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19 SENORX, INC.

20
21 IN THE UNITED STATES DISTRICT COURT
22
23 NORTHERN DISTRICT OF CALIFORNIA
24
25 SAN JOSE DIVISION

26 HOLOGIC, INC., CYTYC CORP., and
27 HOLOGIC L.P.,

28 Plaintiffs,

v.

SENORX, INC.,

Defendant.

SENORX, INC.,

Counterclaimant,

v.

HOLOGIC, INC., CYTYC CORP., and
HOLOGIC L.P.,

Counterdefendants.

CASE NO.: 08-CV-0133 RMW

**DEFENDANT SENORX, INC.'S
OPENING CLAIM
CONSTRUCTION BRIEF**

Date: June 25, 2008
Time: 2:00 p.m.
Courtroom: 6, 4th Floor
Judge: Hon. Ronald M. Whyte

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THE PATENTS IN SUIT

Plaintiffs have asserted infringement of claims from three patents relating to radioactive devices placed in the body to treat diseases such as cancer: U.S. Patent Nos. 5,913,813 (the “’813 patent”), 6,413,204 (the “’204 patent”), and 6,482,142 (the “’142 patent”).

The ’813 and ’204 patents are closely related. They share substantially overlapping descriptions of the claimed devices and common priority and expiration dates. The ’813 and ’204 patents purport to solve “unresolved problems” with prior art devices that occur because the prior art devices place radiation sources “directly adjacent” the tissue. Declaration of Adam D. Harber in Support of SenoRx’s Opening Claim Construction Brief (“Harber Decl.”)¹, Ex. 1 (’813 patent), col. 1:28-31, Ex. 2 (’204 patent), col. 2:14-18. This results in the tissue being “overly ‘hot’ to the point where healthy tissue necrosis may result.” *Id.* The ’813 and ’204 patents claim to solve the problems with the prior devices by using an outer volume, or balloon, that when inflated completely surrounds an inner volume containing radioactive material. This design accomplishes the goal of limiting overexposure of body tissue through two key features incorporated into the claims of both the ’813 and ’204 patents. First, because the intensity of radiation decreases dramatically as the distance from the radiation source increases,² overexposure of tissue close to the device is controlled by placing the radiation source in the inner of the two volumes, which is spaced away from the surrounding tissue by the outer volume. This thereby avoids exposure of the surrounding tissue to extremely high doses of radiation directly adjacent the radiation source. *See* Ex. 4 (*Xoft* Cl. Constr. Order) at 2-3; Ex. 1 (’813 patent), Fig. 4, col. 3:14-38; Ex. 2 (’204 patent), Fig. 7D, col. 5:66-7:28. Second, radiation hot spots are avoided by ensuring that the radiation is delivered uniformly to the tissue surrounding the outer balloon. *See* Ex. 1 (’813 patent), col. 3:27-32; Ex. 2 (’204 patent), Claim 1(d). This uniform dosing is accomplished by providing as an essential feature of the devices claimed in the

¹ All exhibits (“Ex.”) referenced herein are exhibits to the Declaration of Adam D. Harber in Support of SenoRx’s Opening Claim Construction Brief, unless otherwise specified.

² The decrease in radiation occurs as a function of the inverse square of the distance from the source.

1 '813 and '204 patents that “the distance from the [inner] spatial volume and the wall [of the outer
2 balloon] is maintained substantially constant over their entire surfaces.” Ex. 1 ('813 patent), col.
3 1:55-57; *see also* Ex. 2 ('204 patent), col. 5:13-26 (same). As discussed below, this necessarily
4 means that the two volumes must be concentric (*i.e.*, sharing a common center and orientation)
5 and substantially the same shape. These structural requirements – symmetry of shape and
6 constant spacing between the inner and outer volumes – are used to produce the symmetrical
7 isodose curves that are at the core of the '813 and '204 patents, and are required by the asserted
8 claims, as discussed below.

9 The '142 patent, on the other hand, is directed to a device that produces predetermined
10 asymmetric isodose curves. Ex. 3 ('142 patent), col. 2:62-64. Instead of the uniform profile
11 provided by the '813 and '204 patents, the devices of the '142 patent “specifically alter[] the
12 isodose profile for applications where particularly sensitive tissue or other concerns result in a
13 desire to limit the dosage on one or more sides of the device.” *Id.* at col. 6:25-29. This is
14 accomplished by using a radiation source that is asymmetrically placed with respect to the
15 apparatus, or with shielding. *Id.* at col. 2:65-3:36. Again, specific structural requirements are
16 found in the limitations in the claims of the '142 patent, as described below.

17 THE LAW OF CLAIM CONSTRUCTION

18 In construing patent claims, a court should first examine the words of the claims, as “the
19 claims themselves provide substantial guidance as to the meaning of particular claim terms.”
20 *Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) (en banc). “Claims ‘must be read
21 in view of the specification, of which they are a part.’” *Id.* at 1315. Other claims of the patent in
22 question “can also be valuable sources of enlightenment as to the meaning of a claim term.” *Id.*
23 at 1314. Because claim terms are normally used consistently throughout the patent, “the usage
24 of a term in one claim can often illuminate the meaning of the same term in other claims.” *Id.* A
25 patent’s prosecution history may also be relevant when construing a patent’s claims, as the
26 prosecution history is “the complete record of the proceedings before the PTO” when the
27 patentee was applying for the patent. *Id.* at 1317. However, where the prosecution history lacks
28 clarity, it is less reliable and “less useful for claim construction purposes” as compared to the

1 other intrinsic evidence. *Id.* The Federal Circuit also has “authorized district courts to rely on
 2 extrinsic evidence,” including expert and inventor testimony, dictionaries, and learned treatises.
 3 *Id.* While such evidence may “shed useful light on the relevant art,” it is “less significant” and
 4 “less reliable” than the intrinsic record for claim construction. *Id.* at 1317-18.

5 CONSTRUCTION OF THE DISPUTED TERMS³

6 I. THE PERSON OF ORDINARY SKILL IN THE ART.

7 The person of ordinary skill in the art has the skills of both a radiation oncologist and a
 8 medical radiation physicist. Such a person would have a Ph.D. in Physics or Medical Physics
 9 with two or more years of clinical experience, or equivalent training and experience, and/or an
 10 M.D. degree with further training and Board Certification in radiation oncology and at least two
 11 years experience practicing as a radiation oncologist, or equivalent training and experience.
 12 Such a person would have knowledge of and experience in various forms of irradiation,
 13 including external beam radiation therapy and brachytherapy, the history and use of
 14 brachytherapy devices, including balloon brachytherapy devices, to treat tumors and tissue
 15 remaining after the surgical extraction of all or a portion of a tumor in and around both naturally
 16 occurring and surgically created cavities, the physics of brachytherapy procedures, the principles
 17 of radioactivity and an understanding of the effect of radiation on cells. Such a person would
 18 have experience inserting and using brachytherapy devices in a variety of cavities, including the
 19 brain, breast, bladder, rectum and vagina. In addition, such a person would be familiar with
 20 remote afterloader technology and available radiation sources. Declaration of Colin G. Orton
 21 (“Orton Decl.”) ¶ 9.

22
 23 ³ Given the substantial differences between the subject matter claimed in the ’813 and ’204
 24 patents versus that claimed in the ’142 patent, SenoRx has addressed the disputed terms of the
 25 ’142 patent in a separate section of this brief than that addressing the terms of the ’813 and ’204
 26 patents. SenoRx also has included an additional section on the construction of “plurality,” a key
 27 term common to at least one asserted claim in each of the patents, and the subject of a co-
 28 pending motion for summary judgment of non-infringement. Pursuant to the Court’s direction at
 the Case Management Conference, SenoRx has ordered the subsections within each of the
 primary sections by priority. (Although the ’813 and ’204 patents are addressed before the ’142
 patent and plurality claim elements, that was done for purposes of clarity, and SenoRx does not
 mean to imply that the ’142 patent or the plurality elements are of any lesser importance.)

II. THE '813 AND '204 PATENTS.

A. Predetermined Spacing ('813 Patent Claim 1, '204 Patent Claim 3).

An essential requirement of the alleged inventions of the '813 and '204 patents – and the asserted claims of those patents – is the delivery of a uniform dose to the tissue. In other words, it is critical to the claimed inventions that “the absorbed dose within the target tissue at points equidistant from the surface of the outer spatial volume should be substantially uniform in substantially every direction.” Ex. 2 ('204 patent), col. 5:16-19. The asserted claims of the '813 and '204 patents thus require a structure that obtains that uniform dose – two concentric volumes with a predetermined spacing between the wall of the inner volume and the wall of the outer volume. This structure is required by the '813 patent in claim 1's requirement of “a predetermined constant spacing” between the surfaces of the inner volume and outer balloon. Similarly, it is required by the '204 patent in claim 3's requirement of “a predetermined spacing” between the surfaces of the inner volume and outer balloon, and also (as discussed in section B below) by the limitation of claims 1 and 17 to “a three-dimensional isodose profile that is substantially similar in shape” to the outer surface.

1. “Predetermined Constant Spacing” ('813 Patent Claim 1).

Claim Term	SenoRx's Proposed Construction	Plaintiffs' Proposed Construction
predetermined constant spacing between said inner spatial volume and the radiation transparent wall	Fixed spacing, predetermined by one skilled in the art before administering radiation, between the wall or edge of the inner spatial volume and the radiation transparent wall of the outer, closed inflatable chamber, when inflated, which for each point on the wall or edge of the inner spatial volume, the distance to the closest point on the outer chamber is the same (<i>i.e.</i> , the inner spatial volume and outer chamber are concentric and the same shape).	spacing predetermined by one skilled in the art between the wall or edge of the inner spatial volume and the radiation transparent wall of the outer, closed, inflatable chamber, when inflated, which is constant in all directions if the outer chamber is spherical, or constant along a radial plane if the outer chamber is not spherical

SenoRx's proposed construction requires that there be a predetermined fixed distance between the surfaces of the inner and outer volumes. This occurs only when the volumes have the same shape and are concentric (*i.e.*, sharing a common center and orientation), and holds true

1 for any shape of outer balloon. Orton Decl. ¶¶ 25-32. As discussed below, SenoRx's
2 construction is consistent with all the intrinsic evidence relating to this claim limitation.

3 Plaintiffs' proposed construction, on the other hand, incorrectly construes "predetermined
4 constant spacing" in the '813 patent to require different things for differently shaped outer
5 balloons.⁴ For spherical balloons, Plaintiffs state the spacing must be "constant in all directions."
6 While the parties may agree in concept, Plaintiffs' definition does not precisely capture the claim
7 language. SenoRx's proposed construction accurately describes what must be held constant: the
8 distance from any point on the outside surface of the inner spatial volume to the closest point on
9 the wall of the outer surface. For the non-spherical balloons, Plaintiffs' construction is that the
10 spacing need be "constant only along a radial plane." That construction is inconsistent with the
11 intrinsic evidence, which shows the term "constant spacing" means that the walls of the two
12 volumes are spaced equidistant over their entire surfaces. Orton Decl. ¶¶ 26, 30.

13 First, claim element 1(c) of the '813 patent requires "constant spacing" between the inner
14 spatial volume and the radiation transparent wall. It does not say the spacing need be constant
15 only along a single plane, or that it varies depending on the shape of the outer balloon.

16 Second, in the specification, the patentees clearly and repeatedly state that it is important
17 for the spacing of the volumes of their claimed devices to be constant over the entire surfaces of
18 the volumes, not just along a single plane. The abstract for the '813 patent concisely describes
19 the requirement:

20 An instrument for use in brachytherapy comprises a concentric
21 arrangement of inner and outer distensible, spherical chambers
22 disposed near the proximal end of a catheter body An
23 alternative embodiment includes non-spherical inner and outer
chambers whose respective walls are spaced equidistant over the
entire surfaces thereof.

24 Ex. 1 ('813 patent), Abstract (emphases added). With respect to the only non-spherical
25 embodiment (Figure 3), the specification repeats that it is critical that "the spacing between the

26 ⁴ In *Xoft*, Cytac proposed essentially the same construction. Xoft claimed indefiniteness and
27 proposed no construction of its own. The Court rejected the indefiniteness argument and,
28 accordingly, accepted the definition proposed by Cytac. Ex. 4 (*Xoft* Cl. Constr. Order) at 6-7.

1 wall of the inner chamber and the wall of the outer chamber remain generally constant.” *Id.* at
2 col. 3:10-14. Again, the constant spacing is not limited to a single plane. *See also id.* at col.
3 1:55-57 (“[T]he distance from the [inner] spatial volume and the wall [of the outer balloon] is
4 maintained substantially constant over their entire surfaces.”); *id.* at 4:12-15 (“the spacing
5 between the inner and outer chambers needs to be held somewhat constant to avoid ‘hot
6 spots.’”). The embodiments illustrated by the inventors further demonstrate the accuracy of
7 SenoRx’s proposed construction. Figure 1 of the ’813 patent depicts concentric spheres. *See*
8 *also id.* at col. 2:56-63 (the device “may have a solid spherical radiation emitting material in
9 which event that solid sphere would be surrounded with the outer spherical wall”). Figure 3 is
10 non-spherical, but clearly depicts two chambers that are the same shape and concentric, thus
11 allowing “the spacing between the wall of the inner chamber and the wall of the outer chamber
12 [to] remain generally constant[.]” *Id.* at col. 3:10-13.

13 Third, the prosecution history of the ’813 patent also establishes that the inner and outer
14 volumes must be concentric and the same shape, with a fixed spacing between them. In the
15 prosecution of the ’813 patent, Plaintiffs distinguished the prior art Ishiwara patent on the basis
16 that, unlike Ishiwara, the spacing between “the inner and outer radiation transparent walls” of the
17 claimed invention “is constant over the entire surfaces of the two chambers,” not simply constant
18 along a radial plane. Ex. 5 (Sep. 1, 1998 Am., ‘813 Prosecution History) at 6 (emphasis added).
19 Ishiwara, Plaintiffs explained, “teaches away from applicants’ invention given the elongate,
20 cylindrical shape of the radiation source employed and the oblong-shaped outer balloon
21 surrounding it.” *Id.* at 7 (emphasis added). By distinguishing Ishiwara, the inventors made clear
22 that “constant spacing” was required between the entire surfaces of the volumes – not just in the
23 radial plane – and that this holds true even for non-spherical outer surfaces. The inventors also
24 accordingly reemphasized that the shapes of the inner and outer chambers must be the same.

25 Finally, Plaintiffs did not disagree in the *Xoft* case that the two volumes must be
26 concentric and the same shape. There, Plaintiffs described the device of the ’813 patent as “an
27 instrument comprising a concentric arrangement of an inner spatial volume and an outer spatial
28 volume,” and the outer spatial volume of the device of the ’204 patent as “surrounding and

1 concentric with the inner spatial volume.” Ex. 6 (Cytoc Cl. Constr. Br.) at 7, 15 (emphases
 2 added). And at the *Markman* hearing in *Xoft*, Plaintiffs agreed that constant spacing results in
 3 the volumes having the same shape: “if it’s not constantly spaced, if it’s, for example, an oblong
 4 figure in a spherical balloon, then you don’t have a constant distance.” Ex. 7 (*Xoft Markman Tr.*)
 5 at 71:3-5.

6 2. “Predetermined Spacing” (’204 Patent Claim 3).

7 Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
8 Predetermined 9 spacing . . . 10 between said 11 inner spatial 12 volume and the 13 expandable 14 surface element	Fixed spacing, predetermined by one skilled in the art before administering radiation, between the wall or edge of the inner spatial volume and the wall of the expandable surface element, when inflated, which for each point on the wall or edge of the inner spatial volume, the distance to the closest point on the expandable surface element is the same (<i>i.e.</i> , the inner spatial volume and expandable surface element are concentric and the same shape).	the distance between the inner spatial volume and the expandable surface element is determined in advance

15 Although claim 3 of the ’204 patent uses slightly different language than claim 1 of the
 16 ’813 patent (“a predetermined spacing” versus “a predetermined constant spacing”), a person of
 17 ordinary skill in the art would understand the terms identically based on the specification of the
 18 ’204 patent, including the explicit incorporation of the ’813 patent therein. Ex. 2 (’204 patent),
 19 col. 1:10-11; Orton Decl. ¶¶ 25-32. Because the specification of the ’204 patent makes clear that
 20 “predetermined spacing” means the same thing as the closely related term in the parent ’813
 21 patent, SenoRx proposes the same construction for both terms.

22 The ’204 patent teaches that the claimed device should “ensur[e] that the spacing
 23 between the wall of the inner volume and the wall of the outer volume remain[s] generally
 24 constant.” Ex. 2 (’204 patent), col. 5:22-27. The ’204 patent incorporates the embodiments
 25 pictured in the ’813 patent, and the specification of the ’204 patent (like the ’813 patent)
 26 repeatedly emphasizes the constant spacing of the volumes and, consequently, the arrangement
 27 of inner and outer volumes to be the same shape and concentric. *See, e.g., id.* at col. 3:61-65 (the
 28

wall of the volumes are “appropriately spaced” when inflated); 4:61-67 (describing Figure 3 of the ’204 patent as a “solid spherical inner spatial volume” surrounded by an “outer spherical wall”); 5:27-28 (referring to the “concentric spherical embodiment of FIG. 1”).

Plaintiffs’ construction is silent as to what the spacing must be, and only addresses the “predetermined” term.⁵ However, when Plaintiffs addressed the meaning of “predetermined spacing” in the context of the ’204 patent in *Xoft*, Plaintiffs’ expert Dr. Verhey defined it to mean that the “spacing between the inner and outer spatial volumes can be set to a predetermined and constant value.” Ex. 8 (Verhey Decl.) at 10 (emphasis added). Similarly, in addressing claim 4 in *Xoft* (the same claim asserted here), Dr. Verhey opined “the desired shape of the expandable surface element is that shape which provides the predetermined constant spacing between the inner spatial volume and the conformed surface of the resection cavity (see patent 204 5:47-61).” *Id.* at 9 (emphasis added). Thus, the experts on both sides agree the person of ordinary skill in the art would understand the claim term to require constant spacing. *See* Orton Decl. ¶ 25.

Because both claim 1 of the ’813 patent and claim 3 of the ’204 patent require a predetermined constant spacing, SenoRx’s proposed construction should be adopted.

B. Substantially Similar “Three-Dimensional Isodose Profile” (’204 Patent Claims 1, 17).

Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
three-dimensional isodose profile that is substantially similar in shape to the expandable surface element (’204 patent, claim 1);	A final three-dimensional isodose profile that is substantially the same shape as the outer spatial volume expandable surface and is concentric with the outer spatial volume expandable surface.	No construction necessary.
isodose profile having a shape substantially similar to the shape of the outer spatial volume (’204 patent, claim 17)		

⁵ Again, in the *Xoft* case, the Court adopted Plaintiffs’ proposed construction where *Xoft* argued that the claim term was indefinite and proposed no construction of its own. Ex. 4 (*Xoft* Cl. Constr. Order) at 24-25.

1 Plaintiffs have not proposed any construction for this claim element. SenoRx submits it
 2 is proper to instruct the jury as set forth above based on the intrinsic evidence, which compels the
 3 conclusion that the claimed “three-dimensional isodose profile” refers to the final isodose profile
 4 delivered to the tissue. This isodose profile must be substantially the same shape as, and
 5 concentric with (*i.e.*, sharing a common center and orientation), the outer surface. This result
 6 follows from the goal of avoiding the hot spots and radiation overexposure caused by prior art
 7 devices, as illustrated by the specification and prosecution history. *See* Orton Decl. ¶¶ 49-53.

8 **1. “Isodose Profile” Means the Final Absorbed Dose Profile in the**
 9 **Tissue.**

10 The “three-dimensional isodose profile” recited by the claim reflects the final, cumulative
 11 dose of radiation administered by the apparatus to the tissue. Orton Decl. ¶ 50. The stated
 12 purpose of the ’204 patent is to provide an “absorbed dose within the target tissue” that is
 13 “substantially uniform in substantially every direction.” Ex. 2 (’204 patent), col. 5:13-19. The
 14 dose to be delivered is consistently described as the “absorbed dose,” *i.e.*, the final, total resulting
 15 dose from the delivery of radiation absorbed by the tissue at the end of radiation therapy with the
 16 apparatus. Indeed, the focus of the invention is on achieving a “predetermined dose range” in the
 17 target tissue, defined as the dose “between a minimum prescribed absorbed dose for delivering
 18 therapeutic effects to tissue that may include cancer cells, and a maximum prescribed absorbed
 19 dose above which healthy tissue necrosis may result.” Ex. 2 (’204 patent), col. 2:46-55; *see also*,
 20 *e.g.*, *id.* at col. 2:21-26 (“It is desirable to keep the radiation that is delivered to the tissue in the
 21 target treatment region within a narrow absorbed dose range . . .”). This clearly is referring to
 22 the final, cumulative absorbed dose delivered by the device to the tissue, and the “isodose
 23 profile” of claim 1 should be construed accordingly. Orton Decl. ¶ 50.

24 **2. The “Isodose Profile” Must Be Concentric with the Expandable Outer**
 25 **Surface.**

26 In order to obtain their patent in the face of a prior art rejection, the inventors of the ’204
 27 patent added the “substantially similar in shape” limitation to claim 1. Ex. 9 (Dec. 20, 2000
 28 Am., ’204 Prosecution History) at 2, 10-16. In doing so, they described how this limitation
 differentiated their invention from the prior art, and clearly defined what isodose profile meets

1 the “substantially similar in shape” limitation: one that is both substantially similar in shape and
 2 positioned so as to be concentric with (*i.e.*, sharing the same center and orientation) the outer
 3 volume. *Id.*

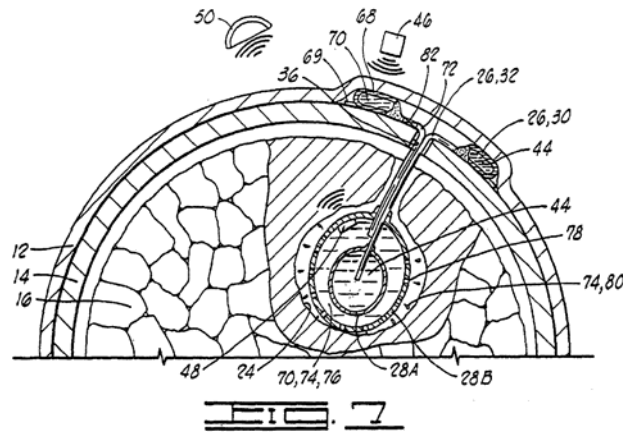
4 There is no dispute that “substantially similar in shape” is an element of the claim. The
 5 dispute is whether the “similarly shaped” isodose profile also must be concentric. This result is
 6 plainly mandated by the patent specification, which discusses the exact relationship between the
 7 dose profile and the outer surface:

8 As illustrated in FIG. 5, it is not essential to the invention that the
 9 volumes 30 and 34 have spherical walls, so long as the resultant
 10 dosing profile is consistent with the shape of the outer volume 34.
 11 That is, the absorbed dose within the target tissue at points
 12 equidistant from the surface 36 of the outer spatial volume 34 should
 13 be substantially uniform in substantially every direction.

14 Ex. 2 (’204 patent), col. 5:13-19 (emphasis added). By definition, if the absorbed dose in the
 15 target tissue equidistant from the surface of the outer spatial volume is substantially the same in
 16 substantially every direction, then the dose profile and the surface must be concentric. Orton
 17 Decl. ¶ 51. The applicants in the prosecution history acknowledged this requirement in
 18 distinguishing the ’204 patent over the prior art (in particular, Figure 7 of the Williams patent,
 19 U.S. Patent No. 5,429,582 (reproduced below)):

20 As seen in Figure 7 of Williams [’582 patent], outer lumen 28B is
 21 not evenly spaced apart from inner lumen 28A that contains the
 22 radiation source. In this system, where the radiation source is
 23 provided as a liquid within the inner balloon, the shape of the three-
 24 dimensional isodose profile will correspond to the shape of the inner
 25 balloon. For this reason, Williams does not provide an apparatus that
 26 can generate a three-dimensional isodose profile that is substantially
 27 similar in shape to the expandable surface element, as is recited in
 28 the claims. That is, because the balloons are not equally spaced
apart, Williams’ apparatus cannot create an isodose profile that has
substantially the same shape as the outer element. Hence, Williams
 fails to disclose each and every limitation of the claimed invention.

Ex. 9 (Dec. 20, 2000 Am., ’204 Prosecution History) at 15-16 (emphases added). Figure 7 of the
 prior art Williams ’582 patent, which the applicants distinguished as non-concentric, appears
 below:



Ex. 10 (Williams '582 patent), Fig. 7. Plainly, the two balloons in Williams (28A and 28B) are the same shape, but not concentric (i.e., sharing a common center and orientation) as the inner balloon is positioned off center from the outer balloon. As a result, the isodose profile generated by this configuration also would not be concentric with the expandable outer surface. Orton Decl. ¶ 52. Because the applicants clearly made the argument that “substantially the same shape” requires concentricity in order to gain allowance of claim 1, the claim limitation must be construed to include concentricity. *See, e.g., Computer Docking Station Corp. v. Dell, Inc.*, 519 F.3d 1366, 1374-75 (Fed. Cir. 2008); *Chimie v. PPG Indus., Inc.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005).

C. “Inner Spatial Volume” ('813 Patent Claim 1; '204 Patent Claim 1).

Claim Term	SenoRx's Proposed Construction	Plaintiffs' Proposed Construction
inner spatial volume	A region of space surrounded by an outer spatial volume that is either enclosed by a <u>distensible</u> polymeric film wall or defined by the outside surface of a solid radionuclide <u>sphere</u> .	A region of space surrounded by an outer spatial volume that is either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide.

The parties' dispute here centers on the physical structure of the inner spatial volume – whether the polymeric film wall must be “distensible” and whether the solid radionuclide must be a “sphere.” In the *Xoft* case, the Court rejected Cytac's proposed construction, and adopted the construction SenoRx proposes here, with the exception that the Court did not include the word “distensible” (and in *Xoft*, neither party addressed the concept). Ex. 4 (*Xoft* Cl. Constr.

Order) at 3-5, 16. Plaintiffs seek to remove the word “sphere” which was part of the Court’s construction in *Xoft*.

1. The “Distensible Polymeric Film Wall” Defining the Inner Spatial Volume.

In the *Xoft* case, this Court concluded that the “inner spatial volume” must be defined by a physical object. *See* Ex. 4 (*Xoft* Cl. Constr. Order) at 5 (“*Xoft* objects that an abstract concept like a region of space cannot be part of an apparatus. *Xoft* is correct. However, the language of the patent does not imply that the inner volume is ever defined by something other than a physical object.”). Because “inner spatial volume” does not specify any structure to one of skill in the art, the Court looked to the specifications of the ’813 and ’204 patents for a definition and concluded that “[i]n all embodiments . . . the boundary of the inner volume is either a polymeric film wall or the edge of a solid sphere.” Ex. 4 (*Xoft* Cl. Constr. Order) at 5; *see also id.* at 16.⁶ Accordingly, the Court construed “inner spatial volume” as an inner volume that is “either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere.” *Id.* at 5, 16.

SenoRx requests that the polymeric film wall be further construed – consistent with the specification and reasoning of the Court’s prior opinion – to be “distensible” (*i.e.*, able to stretch or expand). The patents consistently describe the polymeric film wall used to define the “inner spatial volume” to be distensible. Orton Decl. ¶ 22. For example, in the general discussion of the overall invention, the ’204 patent states: “In different embodiments, the inner spatial volume can be defined by a distensible polymeric wall containing radioactive source material” Ex. 2 (’204 patent), col. 2:56-60 (“Summary of the Invention”) (emphasis added). Similarly, in discussing specific embodiments, the patent specifications make clear that the polymeric film walls must be distensible:

⁶ Neither party here disagrees with the Court’s prior holding in *Xoft* that “inner spatial volume” should be construed consistently across the ’813 and ’204 patents.

- 1 • “With no limitation intended, the distensible polymeric film walls may comprise a
2 biocompatible, radiation resistant polymer” Ex. 2 (’204 patent), col. 3:66-4:3
(emphasis added);
- 3 • “Where the inner and outer spatial volumes are created by inflatable membranes”
4 Ex. 2 (’204 patent), col. 5:22-23 (emphasis added);
- 5 • “where the radiation source is provided as a fluid within an inner balloon” Ex. 2
6 (’204 patent), col. 5:64-65 (emphasis added);
- 7 • “wherein the inner spatial volume is an inner closed, distensible chamber defined by a
8 further radiation transparent wall” Ex. 2 (’204 patent), claim 9 (emphasis added);
- 9 • “inner and outer distensible, spherical chambers” Ex. 1 (’813 patent), Abstract
(emphasis added); and
- 10 • “With no limitation intended, the distensible polymeric chambers may comprise a
11 biocompatible, radiation resistant polymer” Ex. 1 (’813 patent), col. 3:39-41
(emphasis added).⁷

12 Non-distensible polymeric walls are described nowhere in the patents, and were plainly
13 not conceived of or claimed by the inventors as part of their invention. Accordingly, the
14 “polymeric film wall” embodiment of the “inner spatial volume” should be construed to require
15 “distensible” polymeric film walls. Orton Decl. ¶ 22.

16 2. The “Outside Surface of a Solid Radionuclide Sphere” Defining the 17 Inner Spatial Volume.

18 The only radionuclide described as an “inner spatial volume” in the ’813 and ’204 patents
19 is a spherical radionuclide, and the claim term should be construed to require that the
20 radionuclide be spherical. Orton Decl. ¶¶ 23-24. The ’204 patent describes using “a solid
21 spherical radiation emitting material 44 as the inner spatial volume 30. For example, radioactive
22 micro spheres of the type available from the 3M Company of St. Paul, Minn., may be used.” Ex.
23 2 (’204 patent), col. 4:44-50 (emphasis added). Likewise, the ’813 patent states that “a solid
24 spherical radiation emitting material” can be the “inner spatial volume” instead of an inner
25 balloon. Ex. 1 (’813 patent), col. 2:56-63 (emphasis added); *see also id.* at 2:64-65 (“inner
26 spatial volume comprising a single solid sphere”) (emphasis added). In the *Xoft* case, the Court
27

28 ⁷ Emphasis added in each of the bullet points.

1 quoted this portion of the specification in concluding that the inner spatial volume should be
 2 “defined by the outside surface of a solid radionuclide sphere.” Ex. 4 (*Xoft* Cl. Constr. Order) at
 3 5.⁸

4 The description of the radionuclide as spherical was not accidental. As discussed above,
 5 the claimed invention of the ’813 and ’204 patents requires constant spacing between the inner
 6 volume and outer volumes in order to achieve a radiation profile that is “uniform” (Ex. 1 (’813
 7 patent), claim 1) and “substantially similar in shape to the expandable surface element” (Ex. 2
 8 (’204 patent), claim 1). A non-spherical radionuclide will not achieve this result, but instead will
 9 generate a non-uniform dose because of the greater self-absorption of a solid non-spherical
 10 radionuclide in a longitudinal direction than a radial direction. Orton Decl. ¶¶ 23-24.

11 In sum, “inner spatial volume” should be construed to cover that which was described:
 12 the region of space defined by a distensible polymeric film wall or the outside surface of a solid
 13 radionuclide sphere. *See Phillips*, 415 F.3d at 1321 (describing the specification as “the single
 14 best guide to the meaning of a disputed term” because it “acts as a dictionary” when it defines
 15 terms expressly or by implication).

16 **D. “Means . . . For Rendering Uniform” (’813 Patent Claim 1).**

17 Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
18 means . . . for rendering 19 absorbed dose profile of 20 the emissions from the 21 one of the inner spatial 22 volume and outer 23 chamber containing the 24 radionuclides	Function: Making the absorbed dose of radiation substantially more uniform between the surface of the outer chamber and a predetermined depth in the target tissue. Structure: A radiation absorbing or attenuating material, e.g., air, x-ray contrast fluid, contrast media used in angiography, water, a gas, barium sulfate, or their equivalents, that performs this function by absorbing or attenuating radiation.	Function: making the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument Structure: a radiation absorbing or attenuating material, e.g. air, x-ray contrast fluid, contrast media used in angiography, water, a gas, or barium sulfate or their equivalents

26 ⁸ In *Xoft*, *Xoft* proposed a definition that included “spherical.” The Court rejected *Cytac*’s
 27 proposed construction and construed the claim to require that the solid embodiment be a
 28 “sphere.” Ex. 4 (*Xoft* Cl. Constr. Order) at 3-5.

1 Claim element 1(e) of the '813 patent requires "means . . . for rendering uniform the
 2 radial absorbed dose profile." The parties agree this is a means-plus-function claim element, and
 3 that the structure is "a radiation absorbing or attenuating material." The primary dispute between
 4 the parties is whether the "radiation absorbing or attenuating material" must perform the claimed
 5 function by absorbing or attenuating radiation (SenoRx's position), or whether the limitation is
 6 satisfied so long as a "radiation absorbing or attenuating" material is present, even if it does not
 7 render the dose uniform by absorbing or attenuating radiation (Plaintiffs' position).

8 Both parties in the *Xoft* case agreed that uniformity of the dose curve was affected solely
 9 by the distance from the radiation source to the tissue, and not by the radiation absorbing or
 10 attenuating material that occupied the space between the radiation source and the outer balloon.
 11 Accordingly, the Court determined that the material that provided the necessary distance
 12 satisfied the claim element, irrespective of whether it did so as a result of its absorptive
 13 properties. Ex. 4 (*Xoft* Cl. Constr. Order) at 10.

14 SenoRx respectfully disagrees on this key point. The evidence shows that radiation
 15 absorbing or attenuating material in the spatial volumes can, and was meant to, affect the dose
 16 curve. See Orton Decl. ¶¶ 37-38. The specification describes the structure that performs the
 17 function of making the absorbed dose of radiation substantially uniform as "radiation absorbing
 18 fluid," "radioactive ray absorbent material," "radiation absorbing material," and "radiation
 19 attenuation fluid." Ex. 1 ('813 patent), col. 2:50; 2:62-3; 3:27; 1:63; 3:62. The consistent
 20 description of the structure as having this property makes no sense if the structure does not
 21 perform the claimed function as a result of absorbing or attenuating radiation.

22 That the radiation absorbing material must perform the function by absorbing or
 23 attenuating radiation is made clear from the embodiment described at column 3, lines 51-65 of
 24 the '813 patent. In this embodiment, the radioactive material is in the outer balloon, and the
 25 radiation absorbing material is in the inner balloon.⁹ See Ex. 1 ('813 patent), col. 3:51-65.

26
 27 ⁹ This embodiment is within the scope of claim 1. Although asserted claim 11 requires that
 28 the source be in the inner chamber (see claim 8 on which claim 11 depends), claim 1 is not so
 limited. Element (d) of claim 1 states that the radioactive material can be disposed in either the

(continued...)

1 Because of this configuration, the radiation-absorbing material clearly is not performing any
 2 function of spacing the radiation source from the tissue. Nonetheless, the patent describes how
 3 the use of “radiation absorptive material” in the inner chamber can be used to obtain a “uniform
 4 profile” and how “radiation attenuation fluid” in the inner chamber can affect the slope of the
 5 “radial absorbed source gradient.” Ex. 1 (‘813 patent), col. 3:51-65. Thus, in order to have a
 6 construction of the claim that applies to all embodiments, the radiation absorbing or attenuating
 7 material identified by the specification as the “structure” for performing the claimed function
 8 must perform that function by absorbing or attenuating radiation. Orton Decl. ¶ 38.

9 The conclusion that radiation absorbing material may render the dose more uniform, as
 10 the patent states, is scientifically sound. As Dr. Orton explains in detail in paragraphs 37-38 of
 11 his declaration, some of the radiation sources identified in the ‘813 patent at col. 2:51-55 and col.
 12 3:42-8 are relatively low energy sources. The radiation dose delivered from low energy sources
 13 such as those described in the patent can be substantially affected by radiation absorbing
 14 materials. Therefore, the patent contemplated that the radiation absorbing material performed its
 15 function by absorbing radiation, Orton Decl. ¶¶ 37-38, and to satisfy this claim element, the
 16 structure must perform the function by absorbing or attenuating radiation.

17 This reading is further supported by the prosecution history. As in the specification,
 18 Plaintiffs stated the device of their invention used “a radiation attenuating material” to render
 19 uniform the radial absorbed dose profile. Ex. 5 (Sep. 1, 1998 Am., ‘803 Prosecution History) at
 20 4; *see also id.* at 5 (discussing the use of “a substance for rendering uniform the radial absorbed
 21 dose profile”) (emphasis in original). And the Plaintiffs also distinguished the prior art Ishiwara
 22 patent on the grounds that there was “no teaching or suggestion in the patent of how to provide a
 23 uniform radial absorbed dose profile” *Id.* (emphasis in original). If providing such a
 24 profile was a simple matter of spacing the source apart from the tissue (a configuration shown in
 25 Ishiwara), then the distinction made by Plaintiffs would not hold true. In sum, the “radiation

26 _____
 27 (...continued from previous page)
 28 inner or outer chamber, and element (e) states that the “means . . . for rendering uniform” is
 disposed in the other chamber.

absorbing or attenuating material” that the specification clearly links to performing the claimed function must do so by absorbing or attenuating radiation.

The other disputes relating to this element are: 1) whether the dose must be made “substantially more uniform”; and 2) whether the claimed function includes the limitation of preventing over-treatment of body tissue at or close to the balloon wall. As to the first question, SenoRx agrees with the Court that “rendering uniform” the dose in a literal, absolute sense probably is impossible. Ex. 4 (*Xoft* Cl. Constr. Order) at 8-10. That does not mean, however, that “rendering uniform” should be construed to cover rendering the dose “slightly more uniform.” “Substantially more uniform” is consistent the Court’s rationale in the *Xoft* case but is closer to the claim language and the use of the term in the prosecution history. Orton Decl. ¶ 37 n.2. As to the second question, Plaintiffs’ proposed construction provides that the function of making the absorbed dose more uniform is “to prevent over-treatment of body tissue at or close to the outer wall of the instrument.” While “prevent[ing] over-treatment” may in some cases be the result of performing the claimed function, that result is not a part of the claimed function and unnecessary to add.¹⁰

E. “Inner Closed Chamber” (’813 Patent Claim 2).

Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
inner closed chamber	A compartment located completely inside of the outer chamber and closed off within the outer chamber.	No construction necessary.

Claim 2 of the ’813 patent defines the inner spatial volume of claim 1 as an “inner, closed chamber.” Ex. 1 (’813 patent), claim 2. By its plain meaning, this claim further limits the inner spatial volume to a “closed chamber” or compartment located inside of the outer chamber.

Because it is undisputed that the inner spatial volume must be surrounded by the outer spatial

¹⁰ If the Court is inclined to add language concerning the purpose of the function, SenoRx suggests that “to reduce or prevent necrosis in healthy tissue at or close to the outer wall of the instrument” would be more accurate. See discussion at Section F *infra* concerning claim 2 of the ’204 patent.

volume, when the inner spatial volume is an inner closed chamber, it must be completely inside of the outer chamber and closed off within the outer chamber. *See* Orton Decl. ¶ 39.

F. Providing a “Controlled Dose . . . to Reduce or Prevent Necrosis” (’204 Patent Claim 2).

Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface	Controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target tissue so as to reduce or eliminate the risk of damage to healthy tissue in contact with the expandable surface as compared to devices in which the tissue is directly adjacent to the radiation source.	controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target tissue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface.

SenoRx’s proposed construction of this term is more consistent with the plain language of the claim term and the specification than Plaintiffs’ proposed construction.¹¹ The claim specifically refers to “reduc[ing] or prevent[ing] necrosis,” as does the specification. *See* Ex. 2 (’204 patent, col. 7:26-28) (the device allows physicians “to reduce or eliminate the risk of healthy tissue necrosis”). Plaintiffs’ proposed construction, on the other hand, requires avoiding “lethally damag[ing] cells in healthy tissue in contact” with the balloon, a standard found nowhere in the claims or specification, Orton Decl. ¶ 54, and virtually impossible to meet.

III. THE ’142 PATENT

A. “Apparatus Volume” (’142 Patent Claims 1, 6).

Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
apparatus volume	The three-dimensional region of space within the expandable outer surface.	A three-dimensional geometric solid composed of an expandable outer surface.

The meaning of “apparatus volume” was debated at length during the preliminary injunction proceedings in this case. SenoRx stated then, and contends here as well, that the

¹¹ Although the Court construed the term in the manner proposed by Cytac in the *Xoft* case, again *Xoft* argued that the claim was indefinite and did not propose its own definition. Ex. 4 (*Xoft* Cl. Constr. Order) at 23.

1 ordinary and customary meaning of “volume” should apply, and thus the “three-dimensional
2 apparatus volume” is the three-dimensional region of space within the expandable outer surface.

3 In the course of the preliminary injunction proceedings, Plaintiffs initially took the
4 position that the plain meaning of the claim phrase should apply. *See* Pls’ Resp. to SenoRx
5 Interrs. at 9 (Ex. 7 to Docket No. 53) (stating that the term should be given its “Plain meaning
6 (no construction necessary)”). However, Plaintiffs later changed their mind and asserted at the
7 hearing that the terms “apparatus volume” and “expandable outer surface” should be used
8 interchangeably. This construction is repeated here, where Plaintiffs define the apparatus
9 volume as being “composed of an expandable outer surface.”¹² But such a construction is clearly
10 contrary to the language of the claim, the other intrinsic evidence, and the prior position
11 Plaintiffs took regarding the meaning of “volume” in the Xoft litigation. Orton Decl. ¶¶ 55-57.
12 SenoRx respectfully suggests that the claim is not reasonably amenable to the interpretation that
13 the volume is used interchangeably with the surface. *Cf.* Order Denying Plaintiffs’ Motion for
14 Preliminary Injunction (“PI Order”) at 16.

15 **1. The Claims of the ’142 Patent Define the “Apparatus Volume” as a**
16 **Volume, Not a Surface.**

17 The claim construction analysis begins with, and must focus on, the language of the
18 claims themselves. *MSM Invs. Co., LLC v. Carolwood Corp.*, 259 F.3d 1335, 1338-39 (Fed. Cir.
19 2001). Here, the plain meaning of “apparatus volume,” is defined by the claims as the region of
20 space within the expandable outer surface. This region of space “fill[s] [the] interstitial void
21 created by the created by the surgical extraction.” Ex. 3 (’142 patent), claim 1. In filling the
22 surgical cavity, it also necessarily “define[s] an inner boundary of the target tissue to be treated.”
23 *Id.*; Orton Decl. ¶ 56.

24 Plaintiffs’ construction equates “apparatus volume” and “expandable outer surface” and
25 impermissibly rewrites the claim. This results in the first element of the asserted claims being
26 rendered nonsensical. That element requires “an expandable outer surface defining a three-

27 ¹² It is unclear what Plaintiffs mean by “a three-dimensional geometric solid,” a phrase that is
28 found nowhere in the claims, specification, or prosecution history of the ’142 patent.

1 dimensional apparatus volume . . .” Plaintiffs’ construction would have the claims instead read
2 “an expandable outer surface defining an expandable outer surface.” If the phrase “apparatus
3 volume” was meant to be interchangeable with “expandable outer surface,” there would be no
4 need for the language “defining a three-dimensional apparatus volume,” and the claim could
5 simply refer to the “outer surface” throughout. Plaintiffs’ redefinition of apparatus volume –
6 which reads out the “apparatus volume” phrase and the requirement that it must fill the
7 interstitial void – thus runs afoul of the principle that “[a]ll the limitations of a claim must be
8 considered meaningful.” *Unique Concepts, Inc. v. Brown*, 939 F.2d 1558, 1562 (Fed. Cir. 1991);
9 *see also Texas Instruments Inc. v. United States Int’l Trade Comm’n*, 988 F.2d 1165, 1171 (Fed.
10 Cir. 1993) (rejecting a patentee’s proffered claim construction because it “would render the
11 disputed claim language mere surplusage.”).

12 In its denial of Plaintiffs’ Motion for a Preliminary Injunction, this Court raised a
13 possible ambiguity in claim 1, in that it states that the “three-dimensional apparatus volume”
14 could also be read to “define an inner boundary of the target tissue being treated.” From this, the
15 Court concluded that “apparatus volume” may also “refer to the surface of the apparatus, as it is
16 the surface of the balloon that is [in] contact [with] the tissue to be treated and defines the inner
17 margin of tissue to be irradiated.” PI Order at 15. SenoRx respectfully disagrees that the claim
18 language quoted by the Court transforms the “apparatus volume” into the outer surface.

19 In context, there is no inconsistency between the apparatus volume defining an inner
20 boundary of the target tissue and the apparatus volume being a distinct and separate structure from
21 the outer surface (and defined by that surface). The first element of the claim 1 recites, on the
22 Court’s reading, that the apparatus volume (1) fills the void created by surgical extraction of
23 diseased tissue and (2) defines an inner boundary of the target tissue being treated. When devices
24 of this type are used, however, these two functions are two sides of the same coin. When the
25 apparatus volume fills the void left by surgical removal of diseased tissue, the device’s balloon is
26 completely inflated and in contact with the inner boundary of the target tissue. As a result, for all
27 practical purposes, the inner boundary of the target tissue is the same as the outer boundary of the
28 void left after tissue has been removed – both are the edge of the cavity that has been filled by the

1 volume. Accordingly, by filling the void left by the surgical extraction of tissue, the apparatus
 2 volume also necessarily defines an inner boundary of the target tissue to be treated – where the
 3 “filling” of the void stops, the “defining” of the boundary inevitably begins. *See* Orton Decl. ¶ 56.

4 Alternatively, the claim can be read as Plaintiffs do in their infringement contentions, to
 5 the same end. Plaintiffs state:

6 The outer surface of the inflatable spherical Contura™ multi-lumen
 7 balloon (an “expandable surface element”) defines the three-
 8 dimensional apparatus volume that fills the interstitial void of the
 9 resection cavity. The expanded balloon conforms the cavity to the
 10 balloon shape and thereby defines the inner boundary of target tissue
 11 along the cavity wall that is being treated.

12 Ex. 11 (Pls’ Infr. Cont.) at 3. Plaintiffs thus construe claim 1 to mean that the “expandable outer
 13 surface” defines two things: 1) the “three-dimensional apparatus volume that fills the interstitial
 14 void of the resection cavity” and 2) “the inner boundary of the target tissue . . . that is being
 15 treated.” But either way, any ambiguity as to which structure defines the inner boundary of the
 16 target tissue does not affect the plain definition of apparatus volume in the claim. Whether the
 17 boundary of tissue to be treated is defined by the volume or by the surface, the claim plainly
 18 states that the surface defines the volume, and that they are not the same thing. Orton Decl. ¶ 56.

19 **2. Other Intrinsic Evidence Shows the “Apparatus Volume” To Be a** 20 **Volume, Not a Surface.**

21 Plaintiffs’ attempt to define the apparatus volume as the surface also is contrary to the use
 22 of “apparatus volume” in other claims of the ’142 patent (all of which include the limitation of
 23 “an expandable outer surface defining an apparatus volume”). For example, claim 3 requires a
 24 “catheter in communication with the apparatus volume,” and an “elongate member extending
 25 through the catheter into the apparatus volume.” Ex. 3 (’142 patent), claim 3. Under SenoRx’s
 26 construction – that the “apparatus volume” is actually a “volume” – this makes perfect sense.
 27 The catheter is in communication with the volume and can be used to insert the radiation source
 28 into it. Plaintiffs’ construction, on the other hand – that the “apparatus volume” is a “surface” –
 results in the catheter being in communication only with a surface and the elongate member
 extending “into” that surface, which makes no sense. *See CVI/Beta Ventures, Inc. v. Tura LP*,

1 112 F.3d 1146, 1159 (Fed. Cir. 1997) (instructing that terms should be construed consistently
2 throughout the claims).¹³

3 The specification likewise shows that the “apparatus volume” is different from the
4 expandable surface. Thus, the “present invention” of the ’142 patent is stated to have “an
5 expandable outer surface element defining an apparatus spatial volume,” just as in claims 1 and
6 6. Ex. 3 (’142 patent), col. 2:55-64. Specific embodiments describing the apparatus volume and
7 expandable outer surface also do so in such a way that it is clear that the apparatus volume and
8 outer surface are different. *See, e.g., id.* at 3:20-23 (“An interstitial brachytherapy apparatus of
9 the invention may also be implemented in a device having an expandable outer surface defining
10 an apparatus volume”); *id.* at 3:27-32 (“In one embodiment, radiopaque shielding is
11 provided on a portion of the expandable outer surface. In another embodiment, the radiation
12 source is encompassed within a second, inner surface within the apparatus volume”).

13 The prosecution history does not state otherwise. The prosecution history of the ’142
14 patent, as *Phillips* noted is often the case, “lacks the clarity of the specification and thus is less
15 useful for claim construction purposes.” *See Phillips*, 415 F.3d at 1317. But one thing the
16 prosecution history does state, precisely like claims 1 and 6, is that the expandable outer surface
17 and apparatus volume are different: “the expandable outer surface of claims 1 and 9 defines a
18 three-dimensional apparatus volume configured to fill an interstitial void created by the surgical
19 extraction of diseased tissue” Ex. 12 (Mar. 11, 2002 Am., ’142 Prosecution History) at 6.

20 And, as this Court previously has discussed, in the *Xoft* case Plaintiffs argued for – and
21 obtained – precisely the opposite result of what they seek here. There, Xoft sought a
22 construction that the “inner spatial volume” was the inner balloon. Plaintiffs argued that “Xoft
23 confuses the tangible structure that defines the inner spatial volume with the volume itself. The
24 specification provides that the inner spatial volume 30 ‘may be *defined by* a generally spherical
25 polymeric film.’ The film defines the boundary of the volume but the volume is the region of

26
27 ¹³ *See also* claim 4 (member “resuming an asymmetric shape when extended into the
28 apparatus volume”); claim 6 (“two elongate members extending into the apparatus volume”).

1 space within that boundary.” Ex. 6 (Cytoc Cl. Constr. Br.), at 9 (underline emphasis added).
 2 The Court agreed with Plaintiffs, and rejected Xoft’s position: “Xoft’s construction conflates the
 3 boundary of the volume with the volume itself.” Ex. 4 (*Xoft* Cl. Constr. Order), at 5; *see also id.*
 4 at 17. Moreover, the specifications of both the ’813 patent and ’204 patent (and their discussions
 5 of “volumes” being defined by “surfaces”) are explicitly incorporated into the ’142 patent, as are
 6 the concepts of “surfaces” that define “volumes.” *See* Ex. 3 (’142 patent), col. 1:6-12
 7 (“specifically incorporat[ing]” the ’813 and ’204 patents); *see also id.* at 4:28-29 (“outer spatial
 8 volume 30 defined by an outer polymeric film barrier 32”).

9 Accordingly, “apparatus volume” should be construed exactly as Plaintiffs defined it in
 10 their claims: “the three-dimensional region of space within the expandable outer surface.” Orton
 11 Decl. ¶¶ 55-57.

12 **B. “Located So As To Be Spaced Apart from the Apparatus Volume” (’142**
 13 **Patent Claim 1).**

14 Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
15 Located so as to be 16 spaced apart from the apparatus volume	Located outside (<i>i.e.</i> , not within) the apparatus volume.	Located so as to be not on or touching the apparatus volume.

17 The dispute as to meaning of the “spaced apart” limitation mirrors, and substantially is
 18 subsumed by, the argument as to the meaning of apparatus volume. The parties do not appear to
 19 disagree that “located so as to be spaced apart from the apparatus volume” means to be
 20 physically located at a position some distance from the apparatus volume. SenoRx’s
 21 construction of the volume as a region of space means that “spaced apart from the apparatus
 22 volume” is outside the volume, a reading consistent with the plain meaning and other intrinsic
 23 evidence as discussed above. *See* Orton Decl. ¶ 58. Plaintiffs’ construction, on the other hand,
 24 improperly transforms a “region of space” into the physical surface of the balloon that can be
 25 “touched.” SenoRx’s construction should be adopted.

26 **C. “Predetermined Asymmetric Isodose Curves” (’142 Patent, Claims 1, 6, 8).**

27 Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
28		

1 2 3 4 5 6	predetermined asymmetric isodose curves [with respect to the apparatus volume] ('142, claims 1, 8); [within the target tissue] ('142, claim 6)	Isodose curves determined before radiation is administered which are not substantially the same shape as the apparatus volume and/or not concentric with the apparatus volume.	Predetermined isodose curves that are not symmetric with respect to the longitudinal axis of the apparatus volume.
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7 Claim 1 of the '142 patent requires that the radiation source in the device “provide
8 predetermined isodose curves with respect to the apparatus volume.” SenoRx’s construction
9 comports with the language of the claim and requires that the isodose curves must be asymmetric
10 with respect to the “volume.” Orton Decl. ¶ 60. Plaintiffs, on the other hand, improperly seek to
11 read a limitation into the claim found in a few, but not all, of the embodiments of the
12 specification, equating “asymmetric with respect to the apparatus volume” with “not symmetric
13 with respect to the longitudinal axis of the apparatus volume.” Ex. 13 (Pls’ Cl. Constr.) Exhibit
14 C at 4 (emphasis added.)¹⁴; *see also* Orton Decl. ¶ 61.

15 Where the inventors intended to define asymmetry with respect to the longitudinal axis of
16 the device, they did so explicitly. For example, claim 6 requires an elongate member “shaped to
17 provide asymmetric placement of a radiation source with respect to a longitudinal axis through
18 the apparatus volume.” Ex. 3 ('142 patent), claim 6. Claim 1, however, does not include that
19 language. Instead, claim 1 plainly states that the asymmetry is with respect to the “apparatus
20 volume.” Ex. 3 ('142 patent), claim 1. Furthermore, the patent makes clear that, while a
21 “particular” embodiment or configuration might be asymmetric with respect to the longitudinal
22 axis, devices within the scope of the invention were not so limited:

23 The present invention solves the problems described above by
24 providing an interstitial brachytherapy apparatus for delivering
25 radioactive emissions in an asymmetric fashion to target tissue
 surrounding a surgical extraction site. . . . In one configuration,

26 ¹⁴ The parties have not identified any difference with respect to this claim element in claim 1
27 (which states that the curves are “with respect to the apparatus volume”) versus claim 6 (which
28 states that the curves are “within the target tissue”). Thus, both independent claims are
addressed together here.

asymmetric isodose curves are created in the target tissue by shaping or locating the radiation source so as to be asymmetrically placed with respect to a longitudinal axis of the apparatus. . . . In another example, the radiation source comprises a plurality of spaced apart solid radioactive particles disposed within the apparatus volume and arranged to provide a predetermined asymmetric isodose curve within the target tissue.

Ex. 3 ('142 patent), col. 2:56-3:11 (emphasis added); *see also, e.g.*, Ex. 14 (Verhey Depo. Tr.) at 146:13-17 ("Q. Is the radiation profile that is provided by the embodiment of Figure 3 asymmetric with respect to the longitudinal axis of the device? A. No, actually, it's not with respect to the longitudinal axis."). Plaintiffs' attempt to contradict the plain language of its claim in order to read in a limitation from a preferred embodiment – one that would exclude other embodiments that were intended to be covered – should be rejected. *Burke, Inc. v. Bruno Indep. Living Aids, Inc.*, 183 F.3d 1334, 1341 (Fed. Cir. 1999) ("[A]n attribute of the preferred embodiment cannot be read into the claim as a limitation."). SenoRx's construction should be adopted because it is consistent with the claim language and precisely defines "asymmetry" with respect to the apparatus volume. Orton Decl. ¶¶ 60-61.

D. "Asymmetrically Located and Arranged Within the Expandable Surface" ('142 Patent Claim 1).

Claim Term	SenoRx's Proposed Construction	Plaintiffs' Proposed Construction
asymmetrically located and arranged within the expandable surface	Located and arranged inside the expandable surface so as not to be concentric with the expandable outer surface.	Located and arranged so as not to be on the longitudinal axis of the expandable surface.

The parties' positions regarding the "asymmetrically located and arranged within the expandable surface" element substantially track those advanced in connection with the "predetermined asymmetric isodose curves with respect to the apparatus volume." That is, SenoRx's construction states a proper understanding of the plain language of the claim, whereas Plaintiffs again seek to read into the claim a limitation not found in the plain language ("on the longitudinal axis.") The inner spatial volume can be on a longitudinal axis and still be "asymmetrically located" within the meaning of the claim if it is not centered in the balloon. Thus, for the same reasons as stated above, Plaintiffs' construction runs contrary to the specification and the other claims, and should be rejected. *See* Orton Decl. ¶ 59.

1 **IV. “PLURALITY”**

2 **A. “Plurality of Radioactive Solid Particles” / “Plurality of Solid Radiation**
 3 **Sources” (’813 Patent Claim 12; ’204 Patent Claim 17; ’142 Patent Claim 6).**

4 Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
5 Plurality of radioactive 6 solid particles (’813 patent, claim 12)	Two or more separate radioactive solid particles placed in the inner spatial volume at the same time.	No construction necessary
7 Plurality of solid 8 radiation sources (’204 patent, claim 17)	Two or more separate radioactive solid sources placed in the inner spatial volume at the same time.	No construction necessary
9 Plurality of solid 10 radiation sources (’142 patent, claim 6)	Two or more separate radioactive solid sources placed within the expandable outer surface at the same time.	No construction necessary

11 All three patents contain claim terms requiring that a “plurality of radioactive solid
 12 particles” or a “plurality of solid radiation sources” be placed in the inner spatial volume. The
 13 plain meaning of these terms requires that two or more separate radioactive solid sources be
 14 placed in the inner spatial volume at the same time.¹⁵ Orton Decl. ¶¶ 40-41. *See Phillips*, 415
 15 F.3d at 1312-13 (Courts must give words in the claims their ordinary and customary meaning,
 16 which “is the meaning that the term would have to a person of ordinary skill in the art in question
 17 at the time of the invention.”). First, as the Federal Circuit has explained on several occasions,
 18 the term “‘plurality,’ when used in a claim, refers to two or more items, absent some indication
 19 to the contrary.” *Dayco Prods., Inc. v. Total Containment, Inc.*, 258 F.3d 1317, 1327-28 (Fed.
 20 Cir. 2001) (emphasis added); *see also Bilstad v. Wakalopulos*, 386 F.3d 1116, 1122-23 (Fed. Cir.
 21 2004) (affirming Board of Patent Appeals and Interferences’ construction of “plurality” as a
 22 “numerical range . . . bounded by two . . . and . . . infinity”); *York Prods., Inc. v. Central Tractor*
 23

24 ¹⁵ The phrases “radioactive solid particles” and “solid radiation sources” are synonymous.
 25 The terms “particles” and “sources” are used interchangeably in all three patents, *compare* Ex. 3
 26 (’142 patent), col. 3:7-8 (“radiation source comprises a plurality of spaced apart solid radioactive
 27 particles”) *with id.*, col. 9:50-10:1 (“radiation source comprising a plurality of solid radiation
 28 sources”), and all three patents state that “radioactive micro spheres of the type available from
 3M Company of St. Paul, Minn., may be used” as the “solid radioactive particles” or the
 “radioactive source.” *See* Ex. 3 (’142 patent), col. 4:60-62; Ex. 1 (’813 patent), col. 4:1-3; Ex. 2
 (’204 patent), col. 4:49-51.

1 *Farm & Family Ctr.*, 99 F.3d 1568, 1575 (Fed. Cir. 1996) (“The term means, simply, ‘the state
2 of being plural.’”).

3 The intrinsic evidence from all three patents makes clear that “plurality of solid radiation
4 sources” refers to two or more radioactive solid sources. For instance, the specification of the
5 ’813 patent expressly distinguishes a “single” radiation source from a “plurality” of radiation
6 sources: “instead of having the inner spatial volume comprising a single solid sphere, it may
7 instead comprise a plurality of radioactive particles.” Ex. 1 (’813 patent), col. 2:64-66
8 (emphases added). Also, Figure 5 of the ’813 patent depicts a total of five radioactive particles
9 as darkened circles and is described as illustrating an “inner spatial volume occupied by a
10 plurality of radioactive beads that are mounted on the distal ends of a plurality of wires . . . that
11 exit a plurality of ports.” Ex. 1 (’813 patent), col. 3:1-5 (emphasis added). The ’204 patent
12 similarly distinguishes a “plurality” of radiation sources from a “single” source. The
13 specification states that the “inner spatial volume 30, instead of comprising a single solid sphere,
14 may comprise a plurality of radiation emitting particles 44.” Ex. 2 (’204 patent), col. 5:1-4
15 (emphases added); *see also id.* at Fig. 4; col. 3:33-35 (illustrating “an additional embodiment of
16 an interstitial brachytherapy apparatus of the invention having a radiation source comprising a
17 plurality of solid radiation particles” and showing five “radiation emitting particles 44”); Orton
18 Decl. ¶ 41.

19 The same distinction is found in the ’142 patent. In particular, the specification
20 distinguishes “one configuration [in which] asymmetric isodose curves are created . . . by
21 shaping or locating the radiation source so as to be asymmetrically placed” from “another
22 example [in which] the radiation source comprises a plurality of spaced apart solid radioactive
23 particles . . . arranged to provide a predetermined asymmetric isodose curve.” *Compare* Ex. 2
24 (’142 patent), col. 2:65-67 *with id.* at col. 3:7-10.

25 Second, it is equally clear from the intrinsic evidence that the claims require two or more
26 radiation sources to be placed in the inner spatial volume at the same time. Orton Decl. ¶¶ 42-
27 43. The plain language of claim 6 of the ’142 patent provides that at least two radiation sources
28 are simultaneously present when radiation is administered. The claim explicitly requires that

1 “the plurality of radiation sources be[] provided on at least two elongate members extending into
2 the apparatus volume.” Ex. 3 (’142 patent), claim 6. This requirement that the multiple radiation
3 sources be present simultaneously is further emphasized by the plain language of claim 12 of the
4 ’813 patent. Claim 12 depends from claim 1 and specifies that the “radionuclide” of claim
5 limitation 1(d) must “comprise[] a plurality of radioactive solid particles.” *Id.* at claim 12. Thus,
6 without at least two radioactive particles being present at the same time, there is no radionuclide,
7 and limitation 1(d) cannot be satisfied for claim 12. What is claimed is a specific “apparatus,”
8 that must contain a plurality of radiation sources. If a single source is placed into the device,
9 then removed, and then replaced, at no time does the claimed apparatus exist.

10 The specifications of the patents also support SenoRx’s interpretation. The specifications
11 of the ’813 and ’204 patents describe a “plurality of radiation emitting particles” that are
12 “mounted on the distal ends of a plurality of wires . . . and exit a plurality of ports” and explain
13 that the particular “arrangement allows the exact positioning of the individual radiation sources
14 44 to be positioned so as to generate a desired resultant profile.” *See* Ex. 2 (’204 patent), col.
15 5:6-12 (emphasis added); Ex. 1 (’813 patent), col. 3:3-9 (describing “plurality of radioactive
16 beads that are mounted on the distal ends of a plurality of wires . . .”); *see also* Ex. 2 (’204
17 patent), Fig. 4; Ex. 1 (’813 patent), Fig. 5. These teachings therefore make clear that the term
18 “plurality” refers to multiple “individual radiation sources” arranged at the same time.

19 Furthermore, the specification of the ’142 patent teaches that the “resulting asymmetric
20 isodose curve 40 can be further tailored by using solid radioactive particles 36 having differing
21 specific activities to achieve the desired dosing.” *See* Ex. 3 (’142 patent), col. 5:32-35 (emphasis
22 added). This necessarily contemplates that the multiple radiation sources are in the device at the
23 same time because only multiple solid radiation sources could have “differing specific
24 activities.” Orton Decl. ¶ 42. In short, the intrinsic evidence is consistent with the plain meaning
25 that “plurality of solid radiation sources” requires two or more separate radioactive solid sources
26 be placed in the inner spatial volume at the same time.

27 Finally, as Dr. Orton explains, a person of ordinary skill would understand that a device
28 in which a single source was moved around inside an inner spatial volume or removed and

1 inserted into another inner spatial volume to be a very different invention from that described in
 2 these three patents-in-suit, where multiple sources are placed in the instrument at the same time,
 3 and radiation is administered by two or more sources simultaneously. Orton Decl. ¶ 44.

4 **B. “Plurality of Radioactive Solid Particles Placed At Predetermined Locations”**
 5 **(‘813 patent, Claim 12).**

6 Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
7 A plurality of 8 radioactive solid 9 particles placed at predetermined locations (‘813 patent, claim 12)	Two or more separate radioactive solid particles placed in the inner spatial volume at the same time at more than one predetermined location.	No construction necessary

10 Claim 12 of the ‘813 patent requires the “plurality of radioactive particles” to be “placed
 11 at predetermined locations.” Ex. 1 (‘813 patent), claim 12. SenoRx’s proposed construction of
 12 “plurality of radioactive solid particles,” which requires two or more separate radioactive solid
 13 particles placed in the inner spatial volume at the same time, *see* Orton Decl. ¶ 40, is
 14 incorporated into its construction of this phrase. And, the parties have already agreed the term
 15 “predetermined locations” means “more than one predetermined location.” Thus, SenoRx
 16 submits the proper construction of this phrase is “two or more separate radioactive solid particles
 17 placed in the inner spatial volume at the same time at more than one predetermined location.”

18 **C. “Being Provided on At Least Two Elongate Members” (‘142 Patent Claim 6).**

20 Claim Term	SenoRx’s Proposed Construction	Plaintiffs’ Proposed Construction
21 being provided on at 22 least two elongate 23 members extending into the apparatus volume	radiation sources are attached to two or more separate elongate members (e.g. wires or rods) that extend into the three-dimensional region of space within the expandable outer surface at the same time	No construction necessary

24 Claim 6 of the ‘142 patent provides that the plurality of radiation sources are “provided
 25 on at least two elongate members extending into the apparatus volume.” Ex. 3 (‘142 patent),
 26 claim 6. The phrases “provided on” and “at least two” mean the radiation sources are attached to
 27 at least two separate elongate members—e.g., wires—that extend into the outer surface at the
 28 same time. *See, e.g., id.* at Figs. 3 and 4. For the same reasons discussed above regarding

1 “plurality of solid radiation sources,” SenoRx’s proposed construction is consistent with the
 2 plain meaning of the claim and the specification of the ’142 patent. Orton Decl. ¶¶ 62-63.
 3 Reading “provided on at least two elongate members extending into the apparatus volume” to
 4 mean that a single elongate member could be used would eviscerate the plain meaning of the
 5 claim term. Plaintiffs offer no competing construction, presumably intending to rely on the
 6 “plain meaning” of the claim term to assert that a single radionuclide on a single wire, if moved
 7 around, infringes. SenoRx requests that the Court adopt its proposed construction to preclude
 8 any such argument, which is contrary to the plain meaning of the term.

9 CONCLUSION

10 For the foregoing reasons, the Court should adopt SenoRx’s proposed constructions of
 11 the disputed terms of the ’813, ’204, and ’142 patents.

12 Dated: May 21, 2008

Respectfully submitted,

13 By: /s/ F.T.Alexandra Mahaney

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 27 SENORX, INC.
 28

CERTIFICATE OF SERVICE

U.S. District Court, Northern District of California,
Hologic, Inc. et al. v. SenoRx, Inc.
Case No. C-08-0133 RMW (RS)

I, Kirsten Blue, declare:

I am and was at the time of the service mentioned in this declaration, employed in the County of San Diego, California. I am over the age of 18 years and not a party to the within action. My business address is 12235 El Camino Real, Ste. 200, San Diego, CA, 92130.

On May 21, 2008, I served a copy(ies) of the following document(s):

DEFENDANT SENORX, INC.'S OPENING CLAIM CONSTRUCTION BRIEF

on the parties to this action by the following means:

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☒ (BY ELECTRONIC MAIL) I caused such document(s) to be sent via electronic mail (email) to the above listed names and email addresses.

☒ (BY CM/ECF) I caused such document(s) to be sent via electronic mail through the Case Management/Electronic Case File system with the U.S. District Court for the Northern District of California.

I declare under penalty of perjury under the laws of the United States that the above is true and correct, and that this declaration was executed on May 21, 2008.



Kirsten Blue

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18 Attorneys for Defendant and Counterclaimant
19 SENORX, INC.

20
21 IN THE UNITED STATES DISTRICT COURT
22
23 NORTHERN DISTRICT OF CALIFORNIA
24
25 SAN JOSE DIVISION

26 HOLOGIC, INC., CYTYC CORP., and
27 HOLOGIC L.P.,

28 Plaintiffs,

v.

SENORX, INC.,

Defendant.

SENORX, INC.,

Counterclaimant,

v.

HOLOGIC, INC., CYTYC CORP., and
HOLOGIC L.P.,

Counterdefendants.

CASE NO.: 08-CV-0133 RMW

**DECLARATION OF ADAM D.
HARBER IN SUPPORT OF
DEFENDANT SENORX, INC.'S
OPENING CLAIM
CONSTRUCTION BRIEF**

Date: June 25, 2008
Time: 2:00 p.m.
Courtroom: 6, 4th Floor
Judge: Hon. Ronald M. Whyte

1 I, Adam D. Harber, declare that I am an associate at the law firm of Williams & Connolly
2 LLP, admitted pro hac vice to practice before this Court in the above-captioned matter. I serve
3 as outside counsel for Defendant SenoRx, Inc. ("SenoRx"). The following declaration is based
4 on my personal knowledge, and if called upon to testify, I could and would competently testify
5 as to the matters set forth herein.

6 1. Attached hereto as Exhibit 1 is a true and correct copy of U.S. Patent No.
7 5,913,813.

8 2. Attached hereto as Exhibit 2 is a true and correct copy of U.S. Patent No.
9 6,413,204.

10 3. Attached hereto as Exhibit 3 is a true and correct copy of U.S. Patent No.
11 6,482,142.

12 4. Attached hereto as Exhibit 4 is a true and correct copy of the Claim Construction
13 Order (Docket No. 109), from the case captioned Xoft, Inc. v. Cytyc Corp., et al., Case Number
14 C-05-05312 RMW, in the United States District Court for the Northern District of California.

15 5. Attached hereto as Exhibit 5 is a true and correct copy of the September 1, 1998
16 Amendment from the Patent Prosecution History for U.S. Patent No. 5,913,813.

17 6. Attached hereto as Exhibit 6 is a true and correct copy of Cytyc Corporation's
18 (and Hologic's predecessor Proxima Therapeutics') Opening Claim Construction Brief (Docket
19 No. 48), from the case captioned Xoft, Inc. v. Cytyc Corp., et al., Case Number C-05-05312
20 RMW, in the United States District Court for the Northern District of California.

21 7. Attached hereto as Exhibit 7 is a true and correct copy of excerpts of the Claim
22 Construction Hearing (December 20, 2006) from the case captioned Xoft, Inc. v. Cytyc Corp., et
23 al., Case Number C-05-05312 RMW, in the United States District Court for the Northern District
24 of California.

25 8. Attached hereto as Exhibit 8 is a true and correct copy of the Declaration of Lynn
26 J. Verhey, Ph.D. in Support of Cytyc Corporation's Proposed Construction of Claim Terms,
27 Phrases and Clauses (excluding the exhibit cover page and the attached Curriculum Vitae) from
28

1 the case captioned Xoft, Inc. v. Cytoc Corp., et al., Case Number C-05-05312 RMW, in the
2 United States District Court for the Northern District of California.

3 9. Attached hereto as Exhibit 9 is a true and correct copy of the December 20, 2000
4 Amendment from the Patent Prosecution History for U.S. Patent No. 6,413,204.

5 10. Attached hereto as Exhibit 10 is a true and correct copy of U.S. Patent No.
6 5,429,582.

7 11. Attached hereto as Exhibit 11 is a true and correct copy of Plaintiffs' Disclosure
8 of Asserted Claims and Preliminary Infringement Contentions Under Patent Local Rule 3-1.

9 12. Attached hereto as Exhibit 12 is a true and correct copy of the March 11, 2002
10 Amendment from the Patent Prosecution History for U.S. Patent No. 6,482,142.

11 13. Attached hereto as Exhibit 13 is a true and correct copy of Plaintiffs' Preliminary
12 Claim Construction, and Identification of Structure Corresponding to § 112(6) Elements for U.S.
13 Patent Nos. 5,913,813, 6,413,204, and 6,482,142, and Preliminary Identification of Evidence
14 Pursuant to Patent Local Rule 4-2.

15 14. Attached hereto as Exhibit 14 is a true and correct copy of excerpts of the
16 transcript of the Deposition of Lynn Verhey (April 16, 2008).

17
18 I declare under penalty of perjury that the foregoing is true and correct.

19
20 Dated: May 21, 2008

By: 

Adam D. Harber

CERTIFICATE OF SERVICE

U.S. District Court, Northern District of California,
Hologic, Inc. et al. v. SenoRx, Inc.
Case No. C-08-0133 RMW (RS)

I, Kirsten Blue, declare:

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On May 21, 2008, I served a copy(ies) of the following document(s):

**DECLARATION OF ADAM D. HARBER IN SUPPORT OF DEFENDANT
SENORX, INC.'S OPENING CLAIM CONSTRUCTION BRIEF**

on the parties to this action by the following means:

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I declare under penalty of perjury under the laws of the United States that the above is true and correct, and that this declaration was executed on May 21, 2008.



Kirsten Blue

Exhibit 1



US005913813A

United States Patent [19][11] **Patent Number:** **5,913,813****Williams et al.**[45] **Date of Patent:** **Jun. 22, 1999**[54] **DOUBLE-WALL BALLOON CATHETER FOR TREATMENT OF PROLIFERATIVE TISSUE**

5,106,360 4/1992 Ishiware et al. .

5,429,582 7/1995 Williams .

5,611,767 3/1997 Williams .

5,662,580 9/1997 Bradshaw et al. 600/3

5,782,742 7/1998 Crocker et al. .

5,785,688 7/1998 Joshi et al. .

[75] Inventors: **Jeffery A. Williams**, Baltimore, Md.;
Christopher H. Porter, Woodinville,
 Wash.; **Jeffrey F. Williamson**; **James F.**
Dempsey, both of St. Louis, Mo.;
Timothy J. Patrick; **James B. Stubbs**,
 both of Alpharetta, Ga.

[73] Assignee: **Proxima Therapeutics, Inc.**,
 Alpharetta, Ga.

[21] Appl. No.: **08/900,021**[22] Filed: **Jul. 24, 1997**[51] **Int. Cl.⁶** **A61N 5/00**[52] **U.S. Cl.** **600/3**[58] **Field of Search** 600/1-8[56] **References Cited****U.S. PATENT DOCUMENTS**

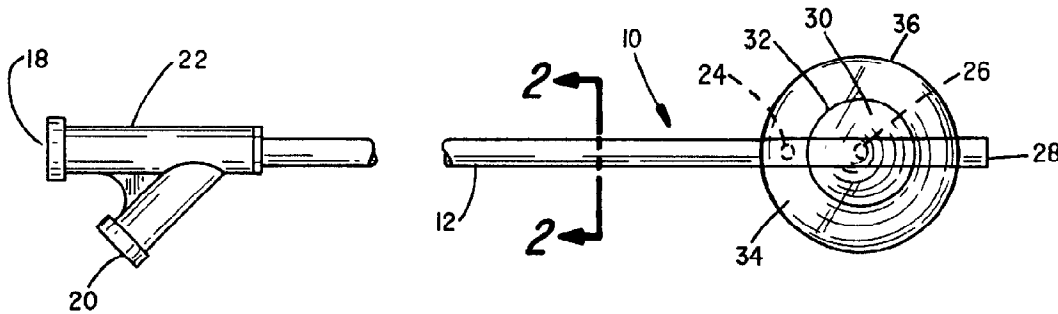
3,324,847 6/1967 Zoumboulis .

Primary Examiner—John P. Lacyk*Attorney, Agent, or Firm*—Nikolai, Mersereau & Dietz, P.A.

[57]

ABSTRACT

An instrument for use in brachytherapy comprises a concentric arrangement of inner and outer distensible, spherical chambers disposed near the proximal end of a catheter body where one of the chambers is made to contain a radioactive material with the other chamber containing a radiation absorptive material, the apparatus functioning to provide a more uniform absorbed dose profile in tissue surrounding a cavity created by the removal of a tumor. An alternative embodiment includes non-spherical inner and outer chambers whose respective walls are spaced equidistant over the entire surfaces thereof.

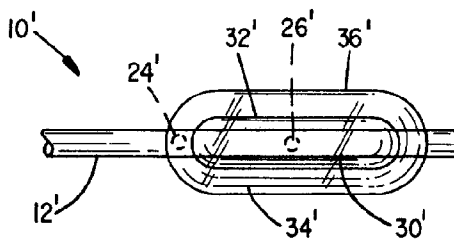
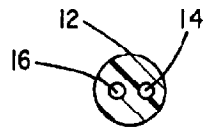
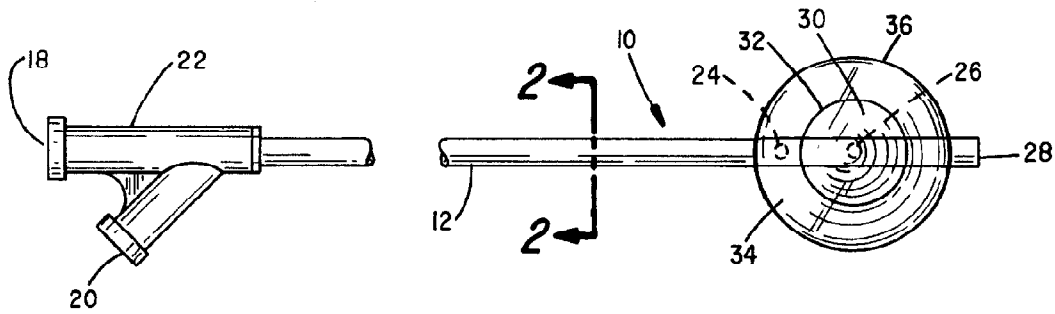
13 Claims, 2 Drawing Sheets

U.S. Patent

Jun. 22, 1999

Sheet 1 of 2

5,913,813



U.S. Patent

Jun. 22, 1999

Sheet 2 of 2

5,913,813

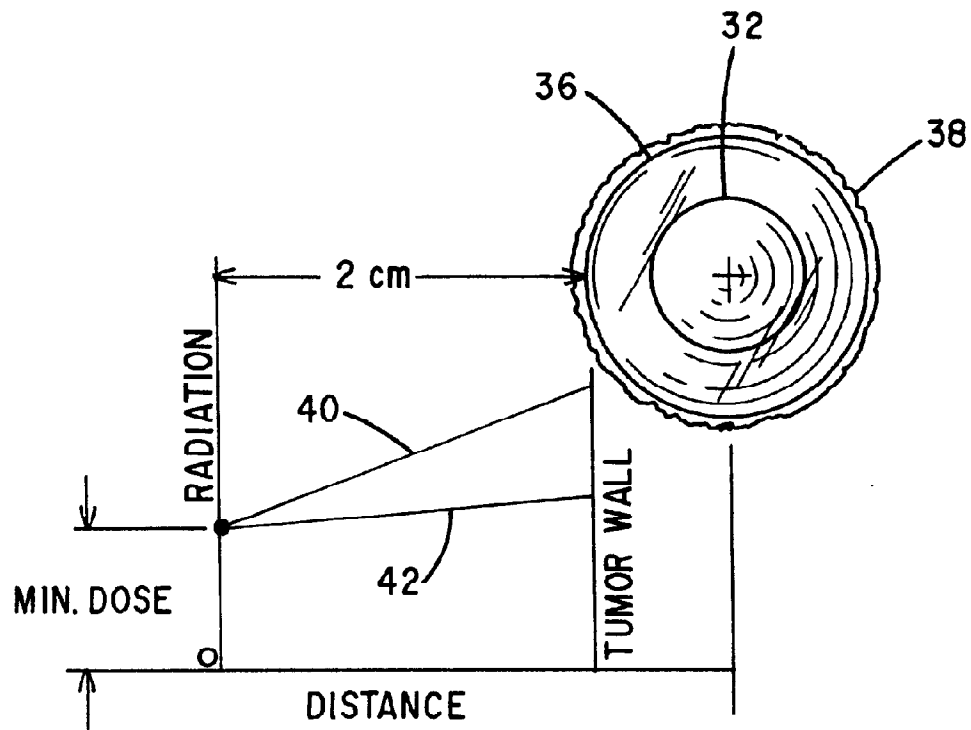


FIG. 4

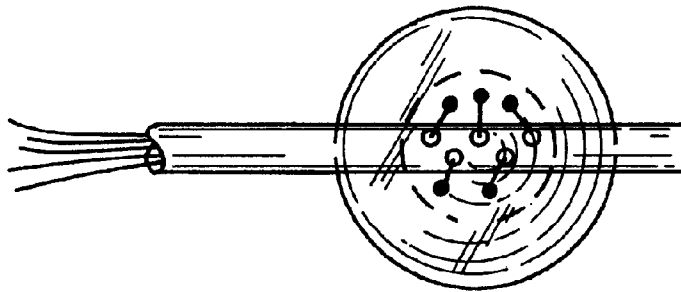


FIG. 5

5,913,813

1

**DOUBLE-WALL BALLOON CATHETER FOR
TREATMENT OF PROLIFERATIVE TISSUE****BACKGROUND OF THE INVENTION****I. Field of the Invention**

This invention relates generally to apparatus for use in treating proliferative tissue disorders, and more particularly to an apparatus for the treatment of such disorders in the body by the application of radioactive material and/or radiation emissions.

II. Discussion of the Prior Art

In the Williams U.S. Pat. No. 5,429,582 entitled "Tumor Treatment", there is described a method and apparatus for treating tissue surrounding a surgically excised tumor with radioactive emissions to kill any cancer cells that may be present in the margins surrounding the excised tumor. In accordance with that patent, there is provided a catheter having an inflatable balloon at a distal end thereof to define a distensible reservoir. Following surgical removal of a tumor, say in the brain or breast, the deflated balloon may be introduced into the surgically-created pocket left following removal of a tumor and then the balloon is inflated by injecting a fluid having radionuclide(s) therein into the distensible reservoir, via a lumen in the catheter.

When it is considered that the absorbed dose rate at a point exterior to the radioactive source is inversely proportional to the square of the distance between the radiation source and the target point, tissue directly adjacent the wall of the distensible reservoir may be overly "hot" to the point where healthy tissue necrosis may result. In general, the amount of radiation desired by the physician is a certain minimum amount that is delivered to a site 0-3 cms away from the wall of the excised tumor. It is desirable to keep the radiation in the space between that site and the wall of the distensible reservoir as uniform as possible to prevent over-exposure to tissue at or near the reservoir wall. In treating other cancers, such as bladder cancer, where the neoplastic tissue is generally located on the bladder surface, deep penetration is unnecessary and to be avoided.

A need exists for an instrument which may be used to deliver radiation from a radioactive source to target tissue within the human body of a desired intensity and at a predetermined distance from the radiation source without over-exposure of body tissues disposed between the radiation source and the target.

SUMMARY OF THE INVENTION

We have found that it is possible to deliver a desired radiation dose at a predetermined radial distance from a source of radioactivity by providing a first spacial volume at the distal end of a catheter and a second spacial volume defined by a surrounding of the first spatial volume by a polymeric film wall where the distance from the spatial volume and the wall is maintained substantially constant over their entire surfaces. One of the inner and outer volumes is filled with either a fluid or a solid containing a radionuclide(s) while the other of the two volumes is made to contain either a low radiation absorbing material, e.g., air or even a more absorptive material, such as an x-ray contrast fluid. Where the radioactive material comprises the core, the surrounding radiation absorbing material serves to control the radial profile of the radioactive emissions from the particular one of the inner and outer volumes containing the radionuclide(s) so as to provide a more radially uniform radiation dosage in a predetermined volume surrounding the

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outer chamber. Where the core contains the absorbent material, the radial depth of penetration of the radiation can be tailored by controlling the core size.

DESCRIPTION OF THE DRAWINGS

The foregoing features, objects and advantages of the invention will become apparent to those skilled in the art from the following detailed description of a preferred embodiment, especially when considered in conjunction with the accompanying drawings in which:

FIG. 1 is a side view of an apparatus for delivering radioactive emissions to body tissue;

FIG. 2 is a cross-sectional view taken along the line 2—2 in FIG. 1;

FIG. 3 is a fragmentary side view of an apparatus for administering radiation therapy in accordance with a second embodiment;

FIG. 4 is a graph helpful in understanding the operation of the apparatus of the present invention; and

FIG. 5 depicts a further embodiment of the invention.

**DESCRIPTION OF THE PREFERRED
EMBODIMENT**

Referring first to FIG. 1, there is indicated generally by numeral 10 a surgical instrument for providing radiation treatment to proliferative tissue in a living patient. It is seen to comprise a tubular body member 12 having first and second lumens 14 and 16 (FIG. 2) extending from proximal ports 18 and 20 in a molded plastic hub 22 to inflation ports 24 and 26 formed through the side wall of the tube 12 and intersecting with the lumens 14 and 16, respectively.

Affixed to the tubular body 12 proximate the distal end 28 thereof is an inner spatial volume 30 which may be defined by a generally spherical polymeric film wall 32. The interior of the chamber 30 is in fluid communication with the inflation port 26. Surrounding the spatial volume 30 is an outer chamber 34 defined by an outer polymeric film wall 36 that is appropriately spaced from the wall 32 of the inner chamber 30 when the two chambers are inflated or otherwise filled and supported. Chamber 34 encompasses the inflation port 24.

The embodiment of FIG. 1 can be particularly described as comprising two spherical chambers 30 and 34, one inside the other. In accordance with a first embodiment of the invention, the outer chamber 34, being the volume defined by the space between the inner spherical wall 32 and the outer spherical wall 36, may be filled with air or, alternatively, a radiation absorbing fluid, such as a contrast media used in angiography. The inner chamber 30 is then filled with a material containing a predetermined radionuclide, for example, I-125, I-131, Yb-169 or other source of radiation, such as radionuclides that emit photons, beta particles or other therapeutic rays.

Those skilled in the art will appreciate that instead of having the inner spatial volume 30 defined by a generally spherical polymeric film wall as at 32, the catheter body member 12 may have a solid spherical radiation emitting material in which event that solid sphere would be surrounded with the outer spherical wall 36 with the spatial volume therebetween occupied by a radioactive ray absorbent material, such as air, water or a contrast material.

It is further contemplated that instead of having the inner spatial volume comprising a single solid sphere, it may instead comprise a plurality of radioactive particles strategically placed within the inner spatial volume so as to radiate

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in all directions with a substantially equal intensity. FIG. 5 illustrates a catheter having the inner spatial volume occupied by a plurality of radioactive beads that are mounted on the distal ends of a plurality of wires that are routed through the catheter body and exit a plurality of ports formed through the wall of the catheter body and reaching the lumen. This arrangement allows the exact positioning of the individual radiation sources to be positioned so as to generate a desired resultant profile.

It is not essential to the invention that the chambers 30 and 34 have spherical walls, so long as the spacing between the wall of the inner chamber and the wall of the outer chamber remain generally constant, such as is illustrated in FIG. 3.

Referring to FIG. 4, there is shown the two concentric spherical chambers of FIG. 1 defined by inner spherical wall 32 and outer spherical wall 36 disposed within the margin 38 of a surgically excised tumor. It is desired that the radiation emitted from the core 32 be capable of delivering a certain minimum dose absorbed at a location approximately 0-3 cms from the margin 38. Curve 40 is a plot of absorbed dose vs. radial distance that would be obtained if the inner chamber defined by spherical wall 32 was not present and the entire volume of the spherical chamber defined by wall 36 were filled with the radioactive fluid. Plot 42 reflects the absorbed dose distribution as a function of radial distance when the radioactive fluid is contained within the inner chamber and is surrounded by either a gas or a more radiation absorbing material. Comparing the plots 40 and 42, by providing the concentric arrangement depicted, the absorbed dose profile in the space between the 2 cm site and the wall of the outer balloon is maintained much more uniform, thus preventing over-treatment of body tissue at or close to the outer wall 36 of the instrument. That is to say, to obtain the same end point absorbed dose at 2 cm, it would be necessary to increase the source activity relative to that used for a completely filled (to surface 36) configuration, assuming the same radionuclide is used in both configurations.

With no limitation intended, the distensible polymeric chambers may comprise a biocompatible, radiation resistant polymer, such as Silastic rubbers, polyurethanes, polyethylene, polypropylene, polyester, PVC, C-Flex. The radioactive fluid contained within the inner chamber 32 can be made from any solution of radionuclide(s), e.g., a solution of I-125 or I-131. A radioactive fluid can also be produced using a slurry of a suitable fluid containing small particles of solid radionuclides, such as Au-198, Y-90. Moreover, the radionuclide(s) can be embodied in a gel.

In the embodiments heretofore described, the material containing the radionuclide(s) is located in the inner chamber. The invention also contemplates that the outer chamber 34 may contain the material having the radionuclide therein while the inner chamber 30 contains the radiation absorptive material. This configuration is advantageous where a profile exhibiting higher intensity at a tissue surface with lesser penetration is desired. By using this approach, less volume of radioactive material is required than if the entire volume of the device were filled with radioactive material. Moreover, the outer chamber wall need not be spherical, yet a uniform profile is obtainable. Experiments have shown that a steeper radial absorbed source gradient can be obtained using a radiation attenuation fluid in the inner chamber 30 than otherwise obtains when only a single distensible chamber is used, as in the aforereferenced Williams U.S. Pat. No. 5,429,582. The invention also contemplates that the radioactive material in the inner core can be replaced by a core containing solid radionuclide-containing

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particles. For example, radioactive micro spheres of the type available from the 3M Company of St. Paul, Minn., may be used in place of the fluid. This radioactive source can either be preloaded into the catheter at the time of manufacture or loaded into the device after it has been implanted into the space formerly occupied by the excised tumor. Such a solid radioactive core configuration offers the advantage in that it allows a wider range of radionuclides than if one is limited to liquids. Solid radionuclides that could be used with the delivery device of the present invention are currently generally available as brachytherapy radiation sources.

In either the concentric spherical embodiment of FIG. 1 or the non-spherical configuration of FIG. 3, the spacing between the inner and outer chambers needs to be held somewhat constant to avoid "hot spots". This result can be achieved by careful placement of precision blown polymer parisons or by using compressible foams or mechanical spacers in the form of webs joining the inner wall 32 to the outer wall 36.

This invention has been described herein in considerable detail in order to comply with the patent statutes and to provide those skilled in the art with the information needed to apply the novel principles and to construct and use such specialized components as are required. However, it is to be understood that the invention can be carried out by specifically different equipment and devices, and that various modifications, both as to the equipment and operating procedures, can be accomplished without departing from the scope of the invention itself.

What is claimed is:

1. Apparatus for delivering radioactive emissions to a body location with a uniform radiation profile, comprising:

- (a) a catheter body member having a proximal end and distal end;
- (b) an inner spatial volume disposed proximate the distal end of the catheter body member;
- (c) an outer, closed, inflatable, chamber defined by a radiation transparent wall affixed to the body member proximate the distal end thereof in surrounding relation to the inner spatial volume with a predetermined constant spacing between said inner spatial volume and the radiation transparent wall;
- (d) a material containing a radionuclide(s) disposed in one of the inner spatial volume and outer chamber; and
- (e) means disposed in the other of the inner spatial volume and outer chamber for rendering uniform the radial absorbed dose profile of the emissions from the one of the inner spatial volume and outer chamber containing the radionuclides.

2. The apparatus as in claim 1 wherein said inner spatial volume is an inner closed, chamber defined by a further radiation transparent wall.

3. The apparatus of claim 1 wherein the means for rendering uniform the absorbed dose profile is a radiation attenuating material.

4. The apparatus of claim 3 wherein the radiation attenuating material is selected from a group consisting of barium sulphate, water, and X-ray contrast media.

5. The apparatus as in claim 2 wherein the radionuclide is in a fluid form.

6. The apparatus as in claim 5 wherein the fluid comprises an isotope of iodine.

7. The apparatus as in claim 1 wherein the radionuclide is a slurry of a fluid containing particles of a solid isotope.

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8. The apparatus as in claim **2** wherein the inner chamber contains the radioactive material.

9. The apparatus as in claim **1** wherein the outer chamber contains the radioactive material.

10. The apparatus as in claim **8** wherein the radioactive material is a fluid.

11. The apparatus as in claim **8** wherein the radioactive material is a solid.

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12. The apparatus as in claim **1** wherein the material containing a radionuclide comprises a plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile.

13. The apparatus as in claim **2** wherein the inner and outer chambers are spherical in shape and are concentric.

* * * * *

Exhibit 2



US006413204B1

(12) **United States Patent**
Winkler et al.

(10) Patent No.: **US 6,413,204 B1**
(45) Date of Patent: ***Jul. 2, 2002**

(54) **INTERSTITIAL BRACHYTHERAPY APPARATUS AND METHOD FOR TREATMENT OF PROLIFERATIVE TISSUE DISEASES**

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(73) Assignee: **Proxima Therapeutics, Inc.**, Alpharetta, GA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **09/293,524**

(22) Filed: **Apr. 15, 1999**

Related U.S. Application Data

(63) Continuation-in-part of application No. 08/900,021, filed on Jul. 4, 1997, now Pat. No. 5,913,813.

(51) Int. Cl.⁷ **A61N 5/00**

(52) U.S. Cl. **600/3**

(58) Field of Search **600/1-8**

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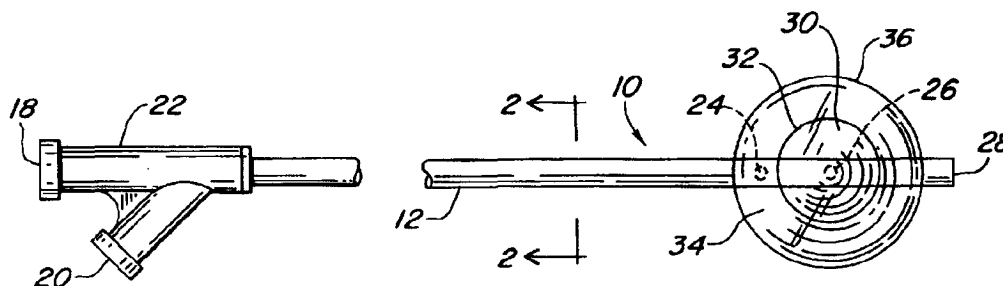
Primary Examiner—John P. Lacyk

(74) Attorney, Agent, or Firm—Thomas J. Engellenner; Ronald E. Cahill; Nutter, McClennen & Fish, LLP

(57) **ABSTRACT**

An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location includes a catheter body member having a proximal end and distal end, an inner spatial volume disposed proximate to the distal end of the catheter body member, an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume, and a radiation source disposed in the inner spatial volume.

36 Claims, 3 Drawing Sheets



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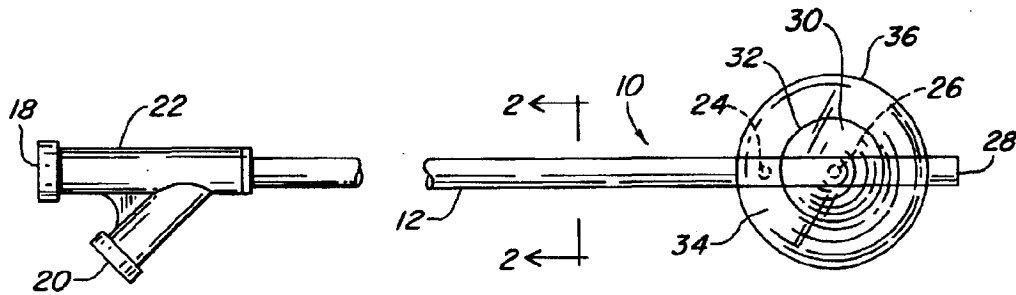


FIG. 1

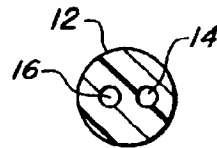


FIG. 2

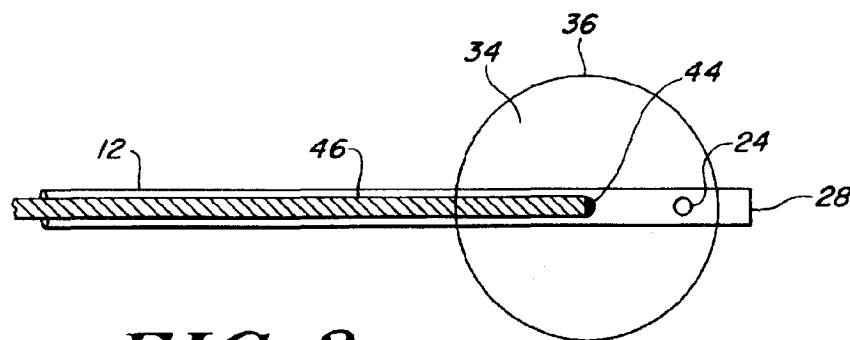


FIG. 3

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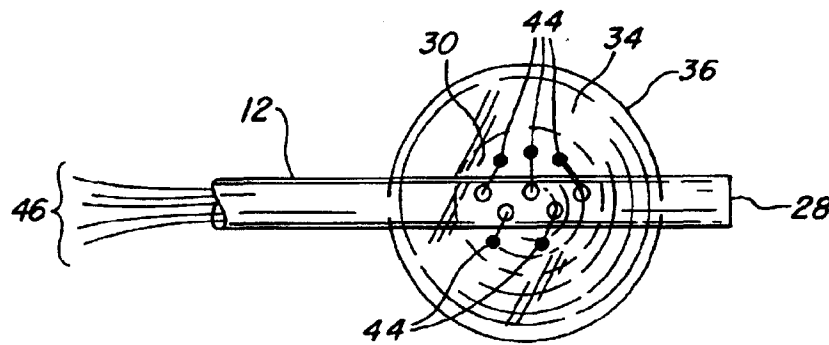


FIG. 4

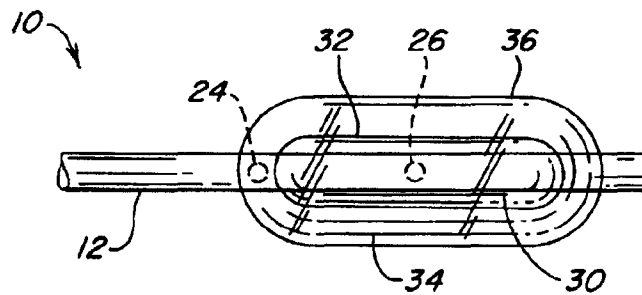


FIG. 5

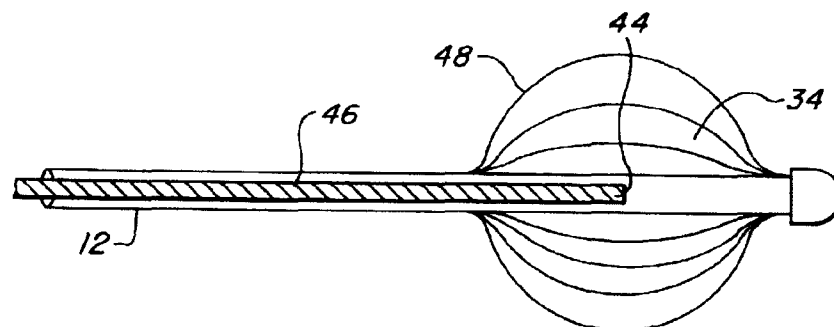


FIG. 6

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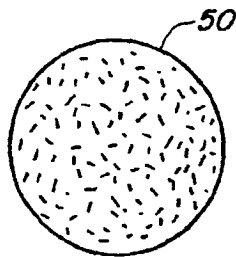


FIG. 7A

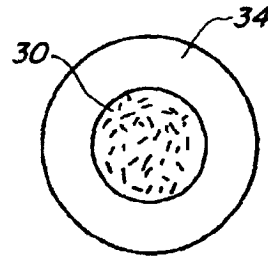


FIG. 7B

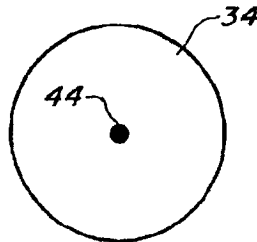


FIG. 7C

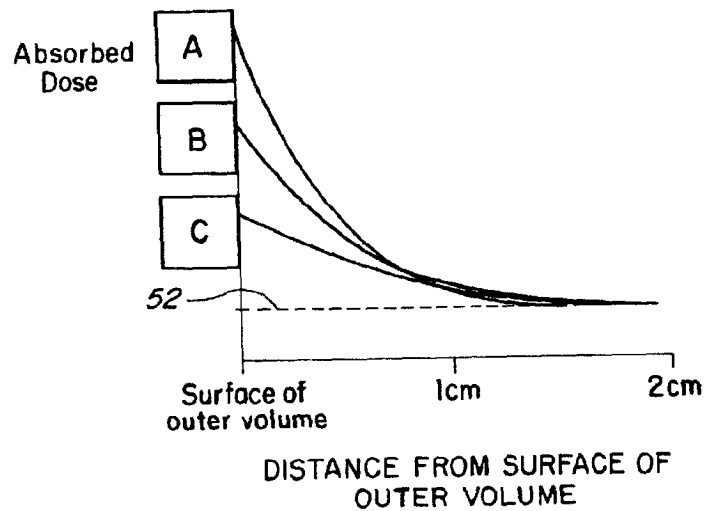


FIG. 7D

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INTERSTITIAL BRACHYTHERAPY APPARATUS AND METHOD FOR TREATMENT OF PROLIFERATIVE TISSUE DISEASES

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. patent application Ser. No. 08/900,021, filed Jul. 24, 1997, now U.S. Pat. No. 5,913,813 the contents of which are specifically incorporated herein by reference.

BACKGROUND OF THE INVENTION

The invention relates generally to apparatus for use in treating proliferative tissue disorders, and more particularly to an apparatus for the treatment of such disorders in the body by the application of radiation.

Malignant tumors are often treated by surgical resection of the tumor to remove as much of the tumor as possible. Infiltration of the tumor cells into normal tissue surrounding the tumor, however, can limit the therapeutic value of surgical resection because the infiltration can be difficult or impossible to treat surgically. Radiation therapy can be used to supplement surgical resection by targeting the residual tumor margin after resection, with the goal of reducing its size or stabilizing it. Radiation therapy can be administered through one of several methods, or a combination of methods, including external-beam radiation, stereotactic radiosurgery, and permanent or temporary interstitial brachytherapy. The term "brachytherapy," as used herein, refers to radiation therapy delivered by a spatially confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site. Owing to the proximity of the radiation source, brachytherapy offers the advantage of delivering a more localized dose to the target tissue region.

For example, brachytherapy is performed by implanting radiation sources directly into the tissue to be treated. Brachytherapy is most appropriate where 1) malignant tumor regrowth occurs locally, within 2 or 3 cm of the original boundary of the primary tumor site; 2) radiation therapy is a proven treatment for controlling the growth of the malignant tumor; and 3) there is a radiation dose-response relationship for the malignant tumor, but the dose that can be given safely with conventional external beam radiotherapy is limited by the tolerance of normal tissue. In brachytherapy, radiation doses are highest in close proximity to the radiotherapeutic source, providing a high tumor dose while sparing surrounding normal tissue. Interstitial brachytherapy is useful for treating malignant brain and breast tumors, among others.

Interstitial brachytherapy is traditionally carried out using radioactive seeds such as ^{125}I seeds. These seeds, however, produce inhomogeneous dose distributions. In order to achieve a minimum prescribed dosage throughout a target region of tissue, high activity seeds must be used, resulting in very high doses being delivered in some regions in proximity to the seed or seeds which can cause radionecrosis in healthy tissue.

Williams U.S. Pat. No. 5,429,582, entitled "Tumor Treatment," describes a method and apparatus for treating tissue surrounding a surgically excised tumor with radioactive emissions to kill any cancer cells that may be present in the tissue surrounding the excised tumor. In order to implement the radioactive emissions, Williams provides a catheter having an inflatable balloon at its distal end that defines a

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distensible reservoir. Following surgical removal of a tumor, the surgeon introduces the balloon catheter into the surgically created pocket left following removal of the tumor. The balloon is then inflated by injecting a fluid having one or more radionuclides into the distensible reservoir via a lumen in the catheter.

The apparatus described in Williams solves some of the problems found when using radioactive seeds for interstitial brachytherapy, but leaves some problems unresolved. The absorbed dose rate at a target point exterior to a radioactive source is inversely proportional to the square of the distance between the radiation source and the target point. As a result, where the radioactive source has sufficient activity to deliver a prescribed dose, say 2 centimeters into the target tissue, the tissue directly adjacent the wall of the distensible reservoir, where the distance to the radioactive source is very small, may still be overly "hot" to the point where healthy tissue necrosis may result. In general, the amount of radiation desired by the physician is a certain minimum amount that is delivered to a region up to about two centimeters away from the wall of the excised tumor. It is desirable to keep the radiation that is delivered to the tissue in the target treatment region within a narrow absorbed dose range to prevent over-exposure to tissue at or near the reservoir wall, while still delivering the minimum prescribed dose at the maximum prescribed distance from the reservoir wall.

There is still a need for an instrument which can be used to deliver radiation from a radioactive source to target tissue within the human body with a desired intensity and at a predetermined distance from the radiation source without over-exposure of body tissues disposed between the radiation source and the target.

SUMMARY OF THE INVENTION

The present invention solves the problems described above by providing an interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location. The apparatus includes a catheter body member having a proximal end and distal end, an inner spatial volume disposed proximate to the distal end of the catheter body member, an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume, and a radiation source disposed in the inner spatial volume. The inner and outer spatial volumes are configured to provide an absorbed dose within a predetermined range throughout a target tissue. The target tissue is located between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface. The predetermined dose range is defined as being between a minimum prescribed absorbed dose for delivering therapeutic effects to tissue that may include cancer cells, and a maximum prescribed absorbed dose above which healthy tissue necrosis may result.

In different embodiments, the inner spatial volume can be defined by a distensible polymeric wall containing radioactive source material which can be a fluid material, by a solid radioactive source, or by a region containing a plurality of solid radioactive sources. The outer spatial volume is defined by an expandable surface element that may be, for example, an inflatable polymeric wall or an expandable cage. The expandable surface element can cause tissue to conform to its intended shape, and preferably, the apparatus creates absorbed isodose profiles in the target tissue that are substantially similar in shape to the expandable surface element in substantially three dimensions.

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The invention also provides a method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location. The method includes surgically creating access to the proliferating tissue within a patient and surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue. An interstitial brachytherapy apparatus for delivering radioactive emissions as described above is then provided and intra-operatively placed into the resection cavity. After a prescribed absorbed dose has been delivered to tissue surrounding the apparatus, the apparatus is removed. The radioactive source material may be placed into the interstitial brachytherapy apparatus after the apparatus is placed in the resection cavity, and may be removed before the apparatus is removed. The method has particular applications to brain and breast cancers.

DESCRIPTION OF THE DRAWINGS

The foregoing features, objects and advantages of the invention will become apparent to those skilled in the art from the following detailed description of a preferred embodiment, especially when considered in conjunction with the accompanying drawings in which:

FIG. 1 is a side view of an interstitial brachytherapy apparatus of the invention for delivering radioactive emissions to body tissue;

FIG. 2 is a cross-sectional view taken along the line 2—2 in FIG. 1;

FIG. 3 is an additional embodiment of an interstitial brachytherapy apparatus of the invention having a solid radiation source;

FIG. 4 is an additional embodiment of an interstitial brachytherapy apparatus of the invention having a radiation source comprising a plurality of solid radiation particles;

FIG. 5 depicts a further embodiment of the invention wherein the inner and outer spatial volumes of the interstitial brachytherapy apparatus are non-spherical;

FIG. 6 illustrates an interstitial brachytherapy apparatus of the invention having an expandable outer spatial volume surface; and

FIGS. 7A–D illustrate the absorbed dose versus distance into target tissue for several interstitial brachytherapy apparatus configurations.

DESCRIPTION OF THE PREFERRED EMBODIMENT

A surgical instrument 10 for providing radiation treatment to proliferative tissue in a living patient is illustrated in FIG. 1. Surgical instrument 10 includes a tubular body member 12 having first and second lumens 14 and 16 (FIG. 2) extending from proximal ports 18 and 20 in a molded plastic hub 22 to inflation ports 24 and 26 formed through the side wall of the tube 12 and intersecting with the lumens 14 and 16, respectively.

Affixed to the tubular body 12 proximate the distal end 28 thereof is an inner spatial volume 30 which may be defined by a generally spherical polymeric film wall 32. The interior of the inner volume 30 is in fluid communication with the inflation port 26. Surrounding inner spatial volume 30 is an outer spatial volume 34 defined by an outer polymeric film wall 36 that is appropriately spaced from the wall 32 of the inner spatial volume 30 when the two volumes are inflated or otherwise supported. Outer volume 34 encompasses inflation port 24. With no limitation intended, the distensible polymeric film walls may comprise a biocompatible, radia-

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tion resistant polymer, such as silastic rubbers, polyurethanes, polyethylene, polypropylene, polyester, or PVC.

The embodiment of FIG. 1 includes inner and outer spatial volumes 30 and 34, one inside the other. The outer spatial volume 34, being the volume defined by the space between the inner spherical wall 32 and the outer spherical wall 36, may be filled with air or, alternatively, a radiation absorbing fluid, such as a contrast media used in angiography. The inner volume 30 is then filled with a material containing a predetermined radionuclide, for example, I-125, I-131, Yb-169 or other source of radiation, such as radionuclides that emit photons, beta particles, gamma radiation, or other therapeutic rays. The radioactive material contained within the inner chamber 32 can be a fluid made from any solution of radionuclide(s), e.g., a solution of I-125 or I-131. A radioactive fluid can also be produced using a slurry of a suitable fluid containing small particles of solid radionuclides, such as Au-198, Y-90. Moreover, the radionuclide(s) can be embodied in a gel. One radioactive material useful in the invention is Iotrex™, a sterile single use, non-pyrogenic solution containing sodium 3-(¹²⁵I)iodo-4-hydroxybenzenesulfonate (¹²⁵I-HBS), available from Proxima Therapeutics, Inc. of Alpharetta, Ga.

As an alternative method of providing radioactive source material, such material may be coated on, chemically bonded to, or copolymerized with the material forming inner spherical wall 32.

Where the radioactive source material is provided as a fluid or gel within inner spherical wall 32, it may be desirable to provide a solid outer spherical wall 36. Should inner spherical wall 32 rupture, the radioactive source material will be retained within outer spherical wall 36 and will not leak into the patient. For further safety, the burst strength of inner spherical wall 32 may be designed so as to be lower than that of outer spherical wall 36. In this way, inner spherical wall 32 will rupture under stress first, releasing its contents into the larger combined space of the inner and outer volumes 30, 34 and releasing any pressure built up within the inner spherical wall 32 and reducing the risk that radioactive material will spill into the patient. In the event of such a rupture, radioactive fluid could be drained from the apparatus through port 24 by way of lumen 14, and also from port 26 by way of lumen 16.

In a further embodiment, illustrated in FIG. 3, instead of having the inner spatial volume 30 defined by a generally spherical polymeric film wall as at 32, the catheter body member 12 may have a solid spherical radiation emitting material 44 as the inner spatial volume 30. For example, radioactive micro spheres of the type available from the 3M Company of St. Paul, Minn., may be used. This radioactive source can either be preloaded into the catheter at the time of manufacture or loaded into the device after it has been implanted into the space formerly occupied by the excised tumor. The solid radiation emitting material 44 can be inserted through catheter 12 on a wire 46, for example, using an afterloader (not shown). Such a solid radioactive core configuration offers an advantage in that it allows a wider range of radionuclides than if one is limited to liquids. Solid radionuclides that could be used with the delivery device of the present invention are currently generally available as brachytherapy radiation sources. In this embodiment solid spherical inner spatial volume 30 is surrounded by outer spherical wall 36, defining outer spatial volume 34 between the outer spherical wall 36 and the inner spatial volume 30 with the outer spatial volume 34 occupied by a radioactive ray absorbent material, such as air, water or a contrast material.

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In a further embodiment, illustrated in FIG. 4, inner spatial volume 30, instead of comprising a single solid sphere, may comprise a plurality of radiation emitting particles 44 strategically placed within the inner spatial volume 30 so as to radiate in all directions with a substantially equal intensity. This plurality of radiation emitting particles 44 can be mounted on the distal ends of a plurality of wires 46 that are routed through the catheter body 12 and exit a plurality of ports formed through the wall of the catheter body and reaching the lumen. This arrangement allows the exact positioning of the individual radiation sources 44 to be positioned so as to generate a desired resultant profile.

As illustrated in FIG. 5, it is not essential to the invention that the volumes 30 and 34 have spherical walls, so long as the resultant dosing profile is consistent with the shape of the outer volume 34. That is, the absorbed dose within the target tissue at points equidistant from the surface 36 of the outer spatial volume 34 should be substantially uniform in substantially every direction. Put another way, the three dimensional isodose profiles generated by the radiation source should be substantially similar in shape to the outer spatial volume 34. Where the inner and outer spatial volumes are created by inflatable membranes and one of the volumes contains a fluid radiation source, this can be achieved by ensuring that the spacing between the wall of the inner volume and the wall of the outer volume remain generally constant. In either the concentric spherical embodiment of FIG. 1 or the non-spherical configuration of FIG. 5, this result can be achieved by careful placement of precision blown or molded polymer partitions or by using compressible foams or mechanical spacers in the form of webs joining the inner wall 32 to the outer wall 36. The desired isodose profiles conforming to the shape of the outer spatial volume 34 can also be obtained, for example, by strategic placement of a plurality of radioactive particle sources within the inner spatial volume 30. Where the apparatus of the invention is deployed in soft tissue, it may also be important for the surface 36 of the outer spatial volume 34 to be sufficiently firm so as to force the target tissue to take on the shape of the surface 36 so that the desired relationship between the isodose profiles and the target tissue is achieved.

When used in an interstitial application, the surface of the outer spatial volume 34 must establish a relationship between the inner spatial volume 30 and the target tissue so as to achieve the aforementioned isodose profile, however, the surface of the outer volume need not be a solid material. For example, as illustrated in FIG. 6, the surface of the outer volume 34 could be an expandable cage 48 formed from a shape memory metal, such as nitinol, or a suitable plastic, such as an expandable polyethylene cage. Such a cage can be formed in the desired shape to conform to a particular isodose profile, then be contracted for delivery to the target site in vivo, then expanded to cause the tissue surrounding the surgically resected region to take the appropriate shape. The size of the outer spatial volume 34 generally will correspond approximately to the amount of tissue resected, or be slightly larger, allowing the expandable surface of the outer spatial volume to urge tissue on the surface of the resected region into the appropriate shape to promote an even dose distribution around the outer spatial volume in the target tissue. In typical applications, the outer spatial volume has a diameter of approximately 2 to 4 centimeters. In these same applications, where the radiation source is provided as a fluid within an inner balloon, the inner balloon generally has a diameter of approximately 0.5 to 3 centimeters.

FIGS. 7A-D illustrate the ability of an interstitial brachytherapy apparatus of the invention to deliver a minimum

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prescribed dose within target tissue while avoiding necrosis inducing radiation "hot spots" in tissue proximate to the apparatus. FIG. 7A illustrates an interstitial brachytherapy apparatus (device A) such as those employed in U.S. Pat. No. 5,429,582, having a single spatial volume 50 filled with a radioactive material in solution. FIG. 7B illustrates an interstitial brachytherapy apparatus (device B) of the invention having a first, inner spatial volume 30 filled with a radioactive material in solution and defined by membrane 32, and a second, outer spatial volume 34 defined by membrane 36 that is substantially evenly spaced apart from membrane 32 in substantially three dimensions. FIG. 7C illustrates an additional interstitial brachytherapy apparatus (device C) of the invention having a solid, spherical radiation source 44 as the inner spatial volume and a spherical outer spatial volume 34 defined by membrane 36.

Each of the devices illustrated in FIGS. 7A-C can be configured to deliver a substantially uniform dose at a given distance into the target tissue from the surface of the outer spatial volume 34 (or from single spatial volume 50 for device A) and to deliver a minimum prescribed dose within a given prescribed depth range into the tissue from the surface of the outer spatial volume 34. However, the different devices provide very different dose profiles as a function of distance from the surface of the outer volume as illustrated in FIG. 7D. FIG. 7D plots the absorbed dose at a given distance into the target tissue from the surface of the outer spatial volume 34 for each of the devices A, B, and C.

Each device can deliver a minimum prescribed dose 52 at a given distance from the surface of the outer spatial volume. For example, device A can readily be configured to provide a dose in a therapeutic range, say between 40 to 60 Gray, at a distance between 0.5 and 1.0 cm from the outer spatial volume for an outer spatial volume having a diameter of 4.0 cm and being in contact with the resection cavity wall. In a typical embodiment, the radioactive source material ranges from approximately 150 to 450 mCi in activity and encompasses most of the target treatment area with a 0.4 to 0.6 Gray/hour isodose contour. At this treatment rate, treatment may be completed in approximately 3 to 7 days, or more commonly, in approximately 3 to 5 days.

In order to reach the minimum prescribed dosage at this distance, however, device A must provide a dose proximate to the surface of the outer spatial volume that is substantially larger than the minimum prescribed dose. For the 4.0 cm diameter outer spatial volume example, the absorbed dosage would be approximately 131 Gray at the outer spatial volume surface. Ideally, radiation therapy should make use of the inherent difference in radiosensitivity between the tumor and the adjacent normal tissues to destroy cancerous tissue while causing minimal disruption to surrounding normal tissues. At high doses of radiation, however, the percentage of exposed cells that survive treatment decreases with first-order kinetics in proportion to increasing radiation dose. With increasing cell death comes increasing risk of necrosis or tissue death in healthy tissue that is treated with a high dose of radiation. Accordingly, it is desirable to keep the maximum radiation dose delivered by the brachytherapy apparatus as low as possible while still delivering the desired therapeutic dose to the desired range of tissue.

Comparing the plots A, B, and C, the absorbed dose profile in the space between the 2 cm site and the surface of the outer spatial volume for the devices of the invention is maintained in a much narrower range, preventing over-treatment of body tissue at or close to the surface of the outer volume of the device. Because devices B and C provide an outer spatial volume 34 between the radioactive source and

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the target tissue, these devices can use hotter radiation sources to reach the minimum prescribed dosage, but take advantage of the distance between the radioactive source and the target tissue provided by the outer spatial volume 34 to reduce or eliminate hot spots in the target tissue.

Returning to the 4.0 cm diameter outer spatial volume example, if the radiation source is contained within an inner spatial volume, say a solid radioactive sphere such as device C, the absorbed dose profile becomes much different. If the radiation source is configured to provide the same 60 Gray dose at 0.5 cm into the target tissue, the absorbed dose at the outer spatial volume surface is only 94 Gray—a significant decrease from the 131 Gray dose for a type A device. In addition, the treatment range for the type C device will be extended under these circumstance as compared to the type A device, delivering a 40 Gray dose beyond 1.0 cm into the target tissue and delivering approximately double the dose at 3.0 cm into the target tissue. In one embodiment, the inner and outer spatial volumes are configured to control the absorbed dose at the outer spatial volume surface so that the absorbed dose is no greater than about 100 Gray while providing a therapeutic absorbed dose into the target tissue at the desired range. The capability of the apparatus of the invention to deliver absorbed doses deeper into the target tissue than prior interstitial brachytherapy devices while controlling the dose in proximity to the apparatus to reduce or eliminate the risk of healthy tissue necrosis allows for the use of brachytherapy in a greater number of cases.

The interstitial brachytherapy apparatus of the invention can be used in the treatment of a variety of malignant tumors, and is especially useful for in the treatment of brain and breast tumors.

Many breast cancer patients are candidates for breast conservation surgery, also known as lumpectomy, a procedure that is generally performed on early stage, smaller tumors. Breast conservation surgery is typically followed by postoperative radiation therapy. Studies report that 80% of breast cancer recurrences after conservation surgery occur near the original tumor site, strongly suggesting that a tumor bed “boost” of local radiation to administer a strong direct dose may be effective in killing any remaining cancer and preventing recurrence at the original site. Numerous studies and clinical trials have established equivalence of survival for appropriate patients treated with conservation surgery plus radiation therapy compared to mastectomy.

Surgery and radiation therapy are the standard treatments for malignant solid brain tumors. The goal of surgery is to remove as much of the tumor as possible without damaging vital brain tissue. The ability to remove the entire malignant tumor is limited by its tendency to infiltrate adjacent normal tissue. Partial removal reduces the amount of tumor to be treated by radiation therapy and, under some circumstances, helps to relieve symptoms by reducing pressure on the brain.

A method according to the invention for treating these and other malignancies begins by surgical resection of a tumor site to remove at least a portion of the cancerous tumor and create a resection cavity. Following tumor resection, but prior to closing the surgical site, the surgeon intra-operatively places an interstitial brachytherapy catheter apparatus, having an inner spatial volume and an outer spatial volume as described above but without having the radioactive source material loaded, into the tumor resection cavity. Once the patient has sufficiently recovered from the surgery, the interstitial brachytherapy catheter is loaded with a radiation source. The radioactive source dwells in the catheter until the prescribed dose of radiotherapy is

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delivered, typically for approximately a week or less. The radiation source is then retrieved and the catheter is removed. The radiation treatment may end upon removal of the brachytherapy apparatus, or the brachytherapy may be supplemented by further doses of radiation supplied externally.

It will be understood that the foregoing is only illustrative of the principles of the invention, and that various modifications can be made by those skilled in the art without departing from the scope and spirit of the invention. All references cited herein are expressly incorporated by reference in their entirety.

What is claimed is:

1. An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:

- (a) a catheter body member having a proximal end and distal end;
- (b) an inner spatial volume disposed proximate to the distal end of the catheter body member;
- (c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
- (d) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

2. The apparatus of claim 1, wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

3. The apparatus of claim 2, wherein a predetermined spacing is provided between said inner spatial volume and the expandable surface element.

4. The apparatus of claim 3, wherein the expandable surface element is adapted to contact tissue surrounding a resected cavity and adapted to conform the tissue to the desired shape of the expandable surface element.

5. The apparatus of claim 2, wherein the minimum prescribed absorbed dose is 40 Gray at a distance of at least one centimeter from the expandable surface element.

6. The apparatus of claim 5, wherein the dose rate in at least a portion of the target tissue is between about 0.4 and 0.6 Gray/hour.

7. The apparatus of claim 5, wherein the maximum absorbed dose delivered to the target tissue is less than 100 Gray.

8. The apparatus of claim 2, wherein the outer spatial volume has a diameter between about two and four centimeters.

9. The apparatus of claim 2, wherein the inner spatial volume is an inner closed, distensible chamber defined by a further radiation transparent wall.

10. The apparatus of claim 9, wherein the radioactive source is in a fluid form.

11. The apparatus of claim 10, wherein the expandable surface element is a solid distensible surface and the outer spatial volume is a closed, distensible chamber and the expandable surface element is a radiation transparent wall.

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12. The apparatus of claim 11, wherein a burst strength of the distensible chamber defining the outer spatial volume is greater than a burst strength of the chamber defining the inner spatial volume.

13. The apparatus of claim 1, wherein the expandable surface element is an expandable cage.

14. The apparatus of claim 13, wherein the expandable cage comprises a shape memory material.

15. The apparatus of claim 14, wherein the expandable cage comprises nitinol.

16. The apparatus of claim 1, wherein the radiation source is a solid radiation source.

17. The apparatus of claim 1, wherein the radiation source is a plurality of solid radiation sources arranged to provide an isodose profile having a shape substantially similar to the shape of the outer spatial volume.

18. The apparatus of claim 2, wherein the prescribed absorbed dose is delivered to the target tissue in substantially three dimensions.

19. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

- (a) surgically creating access to the proliferating tissue in a patient;
- (b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;
- (c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:
 - (i) a catheter body member having a proximal end and distal end;
 - (ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;
 - (iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
 - (iv) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element;
- (d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity until a prescribed absorbed dose has been delivered to tissue surrounding the apparatus; and
- (e) removing the interstitial brachytherapy apparatus.

20. The method of claim 19, further including placing the radioactive source into the interstitial brachytherapy apparatus after the step of placing the apparatus into the tumor resection cavity.

21. The method of claim 19, further including removing the radioactive source from the interstitial brachytherapy apparatus before the step of removing the apparatus.

22. The method of claim 19, wherein the proliferating tissue is a patient's brain.

23. The method of claim 19, wherein the proliferating tissue is a patient's breast.

24. The method of claim 19, further including configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

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25. The method of claim 24, further including providing a predetermined spacing between said inner spatial volume and the expandable surface element.

26. The method of claim 25, wherein the expandable surface element is adapted to contact tissue surrounding a resected cavity and adapted to conform the tissue to the desired shape of the expandable surface element.

27. The method of claim 24, wherein the minimum prescribed absorbed dose is 40 Gray at a distance of at least one centimeter from the expandable surface element.

28. The method of claim 27, wherein the dose rate in at least a portion of the target tissue is between about 0.4 and 0.6 Gray/hour.

29. The method of claim 27, wherein the maximum absorbed dose delivered to the target tissue is less than 100 Gray.

30. The method of claim 24, wherein the outer spatial volume has a diameter between about two and four centimeters.

31. The method of claim 24, wherein the step of configuring the inner and outer spatial volumes includes expanding the inner and outer spatial volumes.

32. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

- (a) surgically creating access to the proliferating tissue in a patient;
- (b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;
- (c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:
 - (i) a catheter body member having a proximal end and distal end;
 - (ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;
 - (iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
 - (iv) a radiation source disposed in the inner spatial volume;
- (d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity;
- (e) configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface; and
- (f) removing the interstitial brachytherapy apparatus.

33. The method of claim 32, wherein the step of configuring the inner and outer spatial volumes includes expanding the inner and outer spatial volumes.

34. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

- (a) surgically creating access to the proliferating tissue in a patient;
- (b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;

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- (c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:
 - (i) a catheter body member having a proximal end and distal end;
 - (ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;
 - (iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
 - (iv) a radiation source disposed in the inner spatial volume;
 - (d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity;
 - (e) adapting the expandable surface element to contact tissue surrounding the resection cavity to conform the tissue to the desired shape of the expandable surface element;
 - (f) delivering a prescribed absorbed dose to tissue surrounding the apparatus; and
 - (g) removing the interstitial brachytherapy apparatus.
35. The method of claim 34, wherein the step of adapting the expandable surface element includes expanding the outer surface volume.

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36. An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:

- (a) a catheter body member having a proximal end and distal end;
- (b) an inner spatial volume disposed proximate to the distal end of the catheter body member;
- (c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
- (d) a radiation source disposed in the inner spatial volume;

wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

* * * * *

Exhibit 3



US006482142B1

(12) **United States Patent**
Winkler et al.

(10) **Patent No.:** **US 6,482,142 B1**
(45) **Date of Patent:** **Nov. 19, 2002**

(54) **ASYMMETRIC RADIATION DOSING
APPARATUS AND METHOD**

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(73) Assignee: **Proxima Therapeutics, Inc.**,
Alpharetta, GA (US)

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

Ravinder, Nath, Ph.D. et al., Development of an ²⁴¹Am Applicator For Intracavitary Irradiation of Gynecologic Cancers, I.J. Radiation Oncology, Biology, Physics, May 1988, vol. 14, No. 5, pp. 969-978.

(21) Appl. No.: **09/464,727**

Primary Examiner—John P. Lacyk

(22) Filed: **Dec. 16, 1999**

(74) Attorney, Agent, or Firm—Thomas J. Engellenner; Ronald E. Cahill; Nutter McClennen & Fish LLP

Related U.S. Application Data

(57) **ABSTRACT**

(63) Continuation-in-part of application No. 09/293,524, filed on Apr. 15, 1999, which is a continuation-in-part of application No. 08/900,021, filed on Jul. 24, 1997, now Pat. No. 5,913,813.

An interstitial brachytherapy apparatus of the invention delivers radioactive emissions in an asymmetric fashion to target tissue surrounding a surgical extraction site. The apparatus includes an expandable outer surface element defining an apparatus spatial volume, a radiation source disposed within the apparatus volume, and a means for providing predetermined asymmetric isodose curves within the target tissue. In one configuration, asymmetric isodose curves are created in the target tissue by shaping or locating the radiation source so as to be asymmetrically placed with respect to a longitudinal axis of the apparatus. In other configurations, asymmetric radiopaque shielding is provided between the radiation source and the target tissue. A surgical procedure using the apparatus is also described.

(51) Int. Cl.⁷ **A61N 5/00**

(52) U.S. Cl. **600/3**

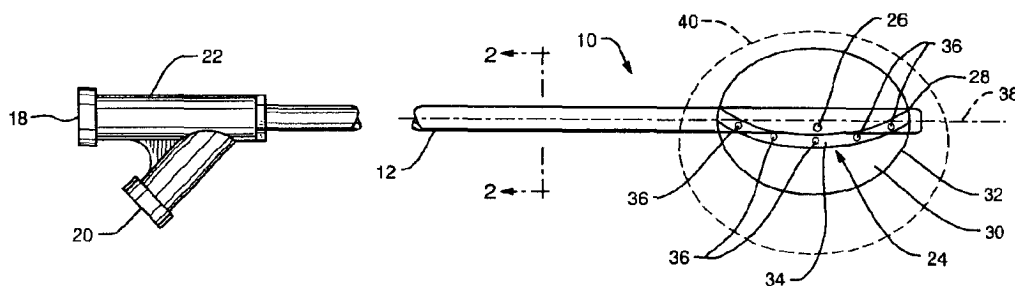
(58) Field of Search 600/1-8

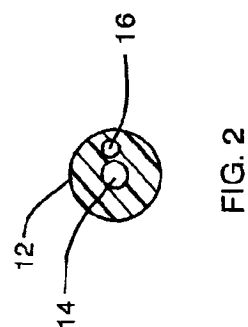
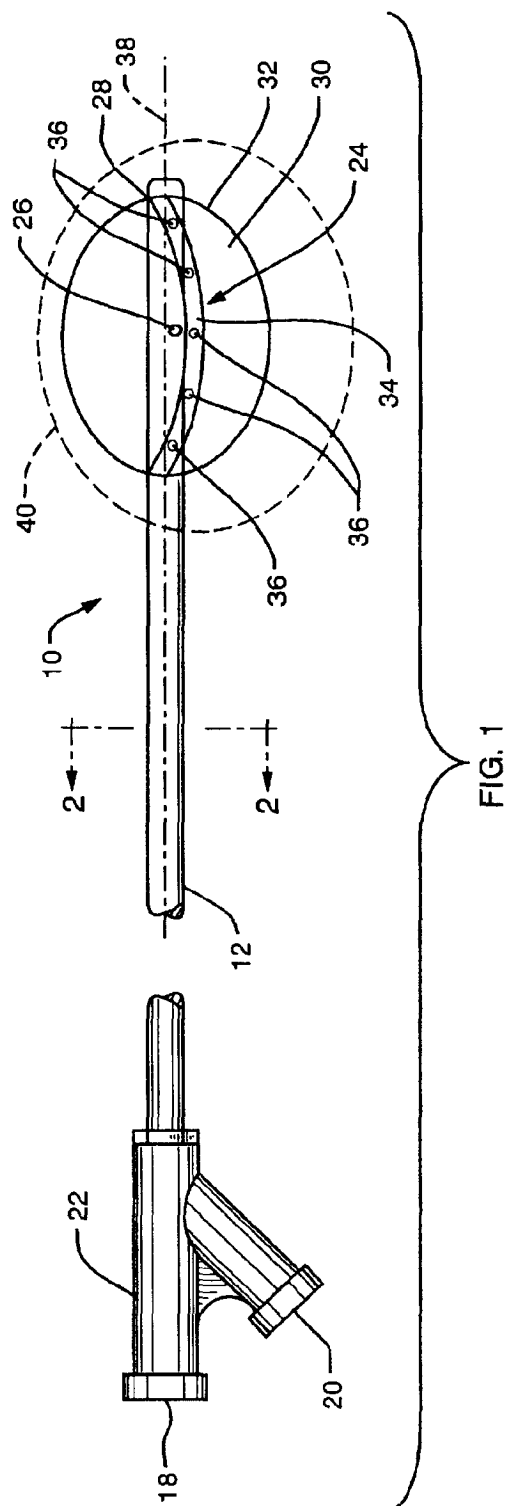
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14 Claims, 4 Drawing Sheets





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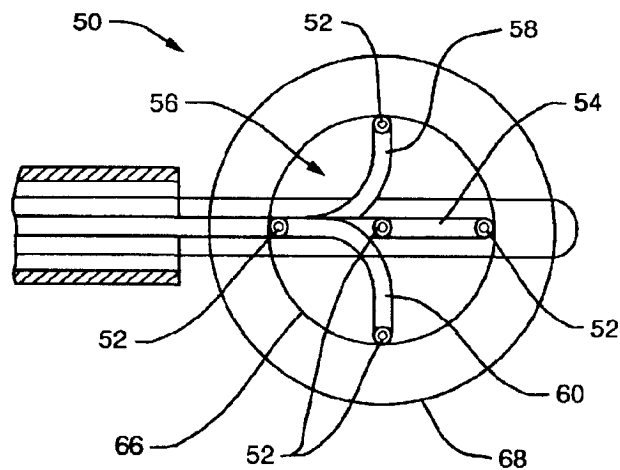


FIG. 3

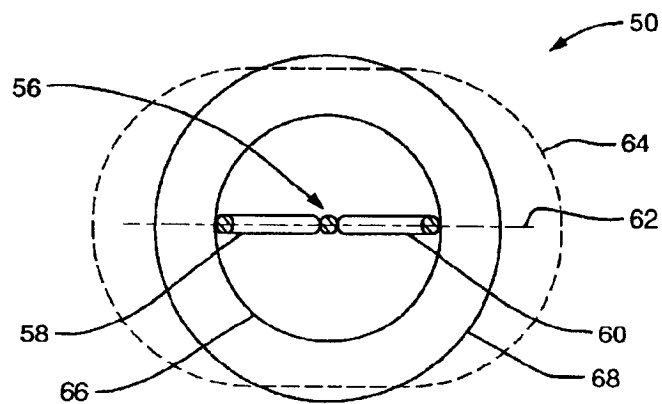


FIG. 3A

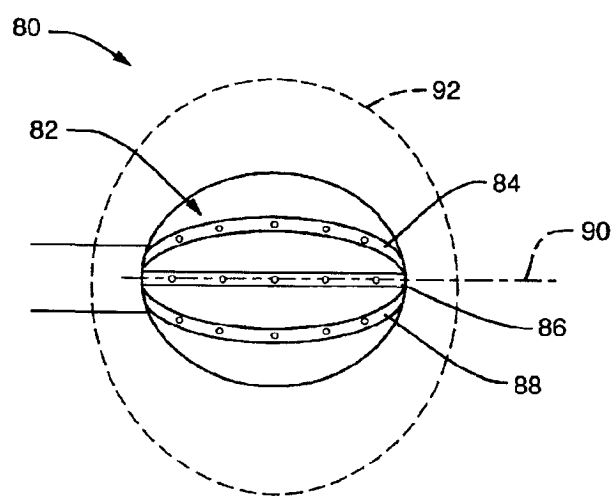


FIG. 4

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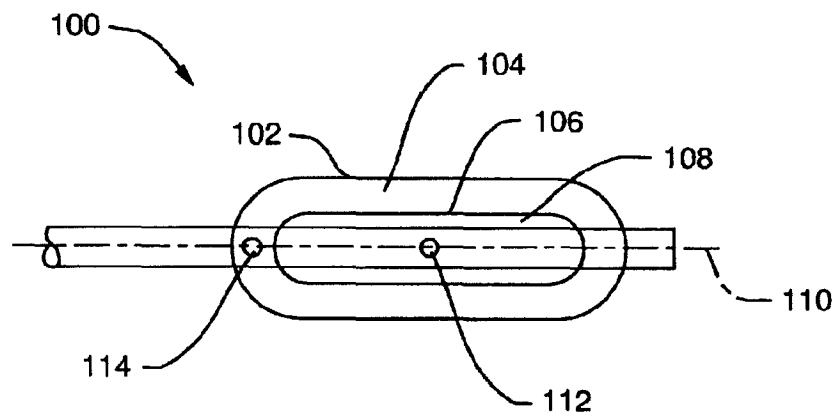


FIG. 5

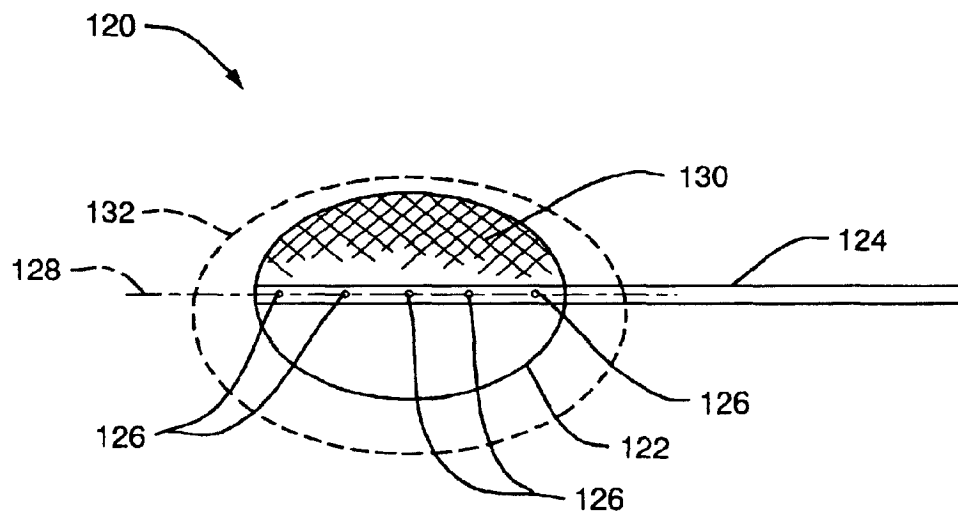


FIG. 6

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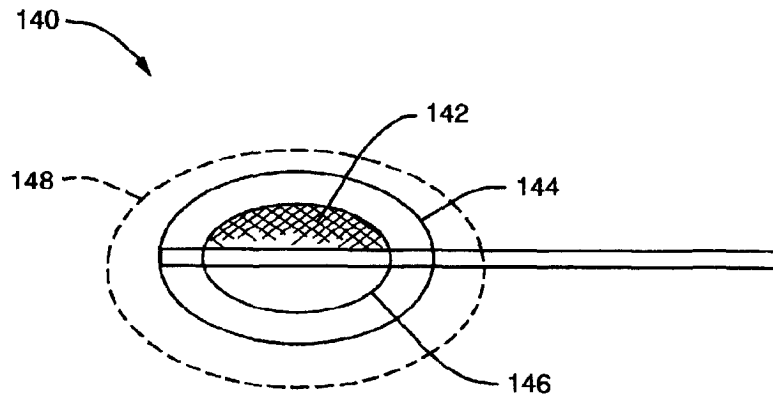


FIG. 7

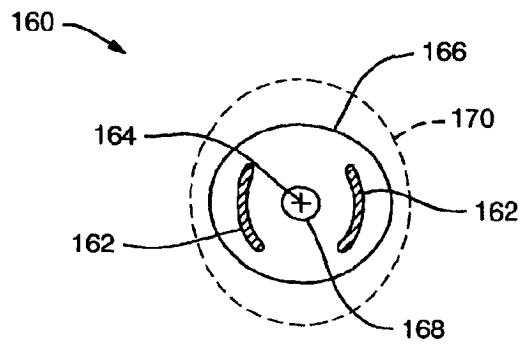


FIG. 8

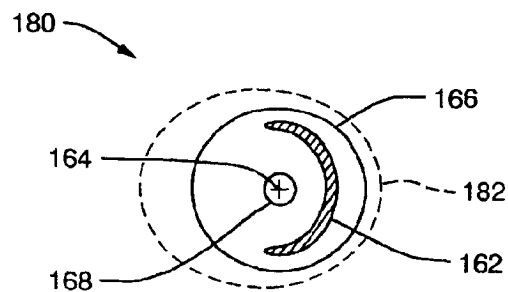


FIG. 9

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ASYMMETRIC RADIATION DOSING APPARATUS AND METHOD

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of co-pending U.S. patent application Ser. No. 09/293,524, filed Apr. 15, 1999, pending which is a continuation-in-part U.S. patent application Ser. No. 08/900,021, filed Jul. 24, 1997 (now issued as U.S. Pat. No. 5,913,813 to Williams et al.); the contents of these applications are specifically incorporated herein by reference.

BACKGROUND OF THE INVENTION

The invention relates generally to an apparatus for use in treating proliferative tissue disorders, and more particularly to an apparatus for the treatment of such disorders in the body by the application of radiation.

Malignant tumors are often treated by surgical resection of the tumor to remove as much of the tumor as possible. Infiltration of the tumor cells into normal tissue surrounding the tumor, however, can limit the therapeutic value of surgical resection because the infiltration can be difficult or impossible to treat surgically. Radiation therapy can be used to supplement surgical resection by targeting the residual tumor margin after resection, with the goal of reducing its size or stabilizing it. Radiation therapy can be administered through one of several methods, or a combination of methods, including external-beam radiation, stereotactic radiosurgery, and permanent or temporary interstitial brachytherapy. The term "brachytherapy," as used herein, refers to radiation therapy delivered by a spatially confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site. Owing to the proximity of the radiation source, brachytherapy offers the advantage of delivering a more localized dose to the target tissue region.

For example, brachytherapy is performed by implanting radiation sources directly into the tissue to be treated. Brachytherapy is most appropriate where 1) malignant tumor regrowth occurs locally, within 2 or 3 cm of the original boundary of the primary tumor site; 2) radiation therapy is a proven treatment for controlling the growth of the malignant tumor; and 3) there is a radiation dose-response relationship for the malignant tumor, but the dose that can be given safely with conventional external beam radiotherapy is limited by the tolerance of normal tissue. In brachytherapy, radiation doses are highest in close proximity to the radiotherapeutic source, providing a high tumor dose while sparing surrounding normal tissue. Interstitial brachytherapy is useful for treating malignant brain and breast tumors, among others.

Interstitial brachytherapy is traditionally carried out using radioactive seeds such as ^{125}I seeds. These seeds, however, produce inhomogeneous dose distributions. In order to achieve a minimum prescribed dosage throughout a target region of tissue, high activity seeds must be used, resulting in very high doses being delivered in some regions in proximity to the seed or seeds which can cause radionecrosis in healthy tissue. One attempt to address this problem, at least with respect to limiting dosages to critical organs near the radioactive seed site, has been to provide a shield directly on a portion of the seed or on an applicator that holds the seed to shield the particularly sensitive tissue. (E.g., Nath et al., Development of an ^{241}Am Applicator for Intracavitary Irradiation of Gynecologic Cancers, *Int'l. J.*

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Radiation Oncology Biol. Phys., Vol., 14, pp. 969-978.) While this approach may be appropriate for some applications, it may still be overly "hot" for treating proximate tissue on the unshielded side of the seed, while not providing an effective dose on the shielded side of the seed.

Williams U.S. Pat. No. 5,429,582, entitled "Tumor Treatment," describes a method and apparatus for treating tissue surrounding a surgically excised tumor with radioactive emissions to kill any cancer cells that may be present in the tissue surrounding the excised tumor. In order to implement the radioactive emissions, Williams provides a catheter having an inflatable balloon at its distal end that defines a distensible reservoir. Following surgical removal of a tumor, the surgeon introduces the balloon catheter into the surgically created pocket left following removal of the tumor. The balloon is then inflated by injecting a fluid having one or more radionuclides into the distensible reservoir via a lumen in the catheter.

The apparatus described in Williams solves some of the problems found when using radioactive seeds for interstitial brachytherapy, but leaves some problems unresolved. The absorbed dose rate at a target point exterior to a radioactive source is inversely proportional to the square of the distance between the radiation source and the target point. As a result, where the radioactive source has sufficient activity to deliver a prescribed dose, say 2 centimeters into the target tissue, the tissue directly adjacent the wall of the distensible reservoir, where the distance to the radioactive source is very small, may still be overly "hot" to the point where healthy tissue necrosis may result. In general, the amount of radiation desired by the physician is a certain minimum amount that is delivered to a region up to about two centimeters away from the wall of the excised tumor. It is desirable to keep the radiation that is delivered to the tissue in the target treatment region within a narrow absorbed dose range to prevent over-exposure to tissue at or near the reservoir wall, while still delivering the minimum prescribed dose at the maximum prescribed distance from the reservoir wall. It is also desirable, at least in some applications, to provide these advantages while tailoring the radiation dosage to avoid fully dosing sensitive tissue or to reduce the amount of radiation that escapes the patient's body.

There is still a need for an instrument which can be used to deliver radiation from a radioactive source to target tissue within the human body with a desired intensity and at a predetermined distance from the radiation source without over-exposure of body tissues disposed between the radiation source and the target, and with the ability to shape the radiation dose to protect sensitive tissue or to protect against radiation exposure outside of the patient's body which may affect healthcare providers or others who might come close to the patient.

SUMMARY OF THE INVENTION

The present invention solves the problems described above by providing an interstitial brachytherapy apparatus for delivering radioactive emissions in an asymmetric fashion to target tissue surrounding a surgical extraction site. The apparatus includes an expandable outer surface element defining an apparatus spatial volume, a radiation source disposed within the apparatus volume, and a means for providing predetermined asymmetric isodose profile within the target tissue.

In one configuration, asymmetric isodose curves are created in the target tissue by shaping or locating the radiation source so as to be asymmetrically placed with respect to a

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longitudinal axis of the apparatus. In one example of an apparatus having this configuration, an inner volume containing a liquid radioisotope is asymmetrically placed within the apparatus volume so as to result in an isodose profile in the target tissue that is asymmetric about the longitudinal axis of the apparatus.

In another example, the radiation source comprises a plurality of spaced apart solid radioactive particles disposed within the apparatus volume and arranged to provide a predetermined asymmetric isodose curve within the target tissue. In one particular example, the plurality of spaced apart radioactive particles are provided on a single elongate member that is shaped so that some of the radioactive particles are farther from the longitudinal axis of the apparatus than others. In other particular examples, a plurality of members carrying radioactive particles are provided with at least one of the members being shaped so as to place at least one radioactive particle asymmetrically with respect to the longitudinal axis of the apparatus.

An interstitial brachytherapy apparatus of the invention may also be implemented in a device having an expandable outer surface defining an apparatus volume, a radiation source disposed within and spaced apart from the expandable outer surface, and at least one asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shielding resulting in predetermined asymmetric isodose curves within the target tissue. In one embodiment, radiopaque shielding is provided on a portion of the expandable outer surface. In another embodiment, the radiation source is encompassed within a second, inner surface within the apparatus volume, with radiopaque shielding provided on at least a portion of the inner surface. In still further embodiments, one or more radiation shields are spaced apart from the radiation source and within the apparatus volume to achieve the desired asymmetric isodose distribution within the target tissue.

The invention also provides a method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location. The method includes surgically creating access to the proliferating tissue within a patient and surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue. An interstitial brachytherapy apparatus for delivering radioactive emissions as described above is then provided and intra-operatively placed into the resection cavity. After a prescribed absorbed dose has been delivered to tissue surrounding the apparatus, the apparatus is removed. The radioactive source material may be placed into the interstitial brachytherapy apparatus after the apparatus is placed in the resection cavity, and may be removed before the apparatus is removed. The method has particular applications to brain and breast cancers.

DESCRIPTION OF THE DRAWINGS

The foregoing features, objects and advantages of the invention will become apparent to those skilled in the art from the following detailed description of a preferred embodiment, especially when considered in conjunction with the accompanying drawings in which:

FIG. 1 is a side view of an interstitial brachytherapy apparatus of the invention for delivering asymmetric radioactive doses to body tissue;

FIG. 2 is a cross-sectional view taken along the line 2—2 in FIG. 1;

FIG. 3 is a side view of an additional embodiment of an interstitial brachytherapy apparatus of the invention;

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FIG. 3A is an end view of the interstitial brachytherapy apparatus of FIG. 3;

FIG. 4 is a side view of an additional embodiment of an interstitial brachytherapy apparatus of the invention;

FIG. 5 is a side view of an interstitial brachytherapy apparatus of the invention configured for use with a liquid radiation source.

FIG. 6 is a side view of an interstitial brachytherapy device of the invention employing radiopaque coatings;

FIG. 7 is a side view of an interstitial brachytherapy device of the invention employing radiopaque coating and a liquid radiation source; and

FIGS. 8 and 9 are end views of interstitial brachytherapy devices of the invention employing radiopaque shields.

DESCRIPTION OF THE PREFERRED EMBODIMENT

A surgical instrument 10 for providing radiation treatment to proliferative tissue in a living patient is illustrated in FIG. 1. Surgical instrument 10 includes a tubular body member 12 having first and second lumens 14 and 16 (FIG. 2) extending from proximal ports 18 and 20 in a molded hub 22. The first lumen 14 carries a radioactive source 24 and second lumen 16 communicates with inflation port 26 formed through the side wall of the tube 12.

Affixed to the tubular body 12 proximate the distal end 28 thereof is an outer spatial volume 30 defined by an outer polymeric film barrier 32 that is appropriately spaced from the radioactive source 24. Outer volume 30 encompasses inflation port 26. With no limitation intended, the distensible polymeric film walls may comprise a biocompatible, radiation resistant polymer, such as silastic rubbers, polyurethanes, polyethylene, polypropylene, polyester, or PVC. The outer spatial volume 30 may be filled with air, saline or, alternatively, a radiation absorbing fluid, such as a contrast media used in angiography. Alternatively, the surface of outer volume 30 need not be a solid material. For example the surface of the outer volume 30 could be an expandable cage formed from a shape memory metal, such as nitinol, or a suitable plastic, such as an expandable polyethylene cage. Such a cage can be formed in the desired shape to conform to a particular isodose profile, contracted for delivery to the target site in vivo, then expanded to cause the tissue surrounding the surgically resected region to take the appropriate shape. The size of the outer spatial volume 30 generally will correspond approximately to the amount of tissue resected. For some applications, the size of the outer spatial volume 30 may be slightly smaller than the resected volume while for other applications, the outer spatial volume will be slightly larger than the resected volume, allowing the expandable surface of the outer spatial volume to urge tissue on the surface of the resected region into the appropriate shape to promote an even dose distribution around the outer spatial volume in the target tissue. In typical applications, the outer spatial volume has a diameter of approximately 2 to 6 centimeters.

Radiation source 24 comprises a wire 34 having one or more solid radioactive particles 36 located on the wire 34. For example, radioactive micro spheres of the type available from the 3M Company of St. Paul, Minn., may be used as the solid radioactive particles. Such a solid radioactive particle configuration offers an advantage in that it allows a wider range of radionuclides than if one is limited to liquids. Solid radionuclides that could be used with the delivery device of the present invention are currently generally available as brachytherapy radiation sources. Examples of

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radioactive materials which can be selected by a person of ordinary skills in the art for use with the present invention may be found in Tables 1 to 4 of PCT Publication WO 97/19723, which is hereby incorporated by reference.

The, radioactive source 24 can either be preloaded into the catheter at the time of manufacture, or loaded into the device after it has been implanted into the space formerly occupied by the excised tumor. If loaded after implantation, the solid radiation emitting material 36 can be inserted through lumen 14 on a wire 34, for example using an afterloader (not shown).

Radiation source 24 has an asymmetric configuration with respect to a longitudinal axis 38 of the instrument 10. That is, radiation source 24 is shaped so as to result in an isodose profile 40 that varies radially about the longitudinal axis 38. More simply, the isodose profile 40 of FIG. 1 has a shorter radius from the longitudinal axis 38 on the top side of the instrument 10 as shown in FIG. 1 than on the bottom side. The asymmetrically shaped isodose curve 40 may be created by providing a plurality of solid radioactive particles 36 on a curved wire 34 in a spaced apart relationship. This configuration will result in certain of the solid radioactive particles 36 being farther from the longitudinal axis 38 of the instrument 10 than others, and will result in the illustrated asymmetric isodose profile 40. One way to provide the illustrated radioactive source 24 configuration is to form wire 34 from a solid or tubular shape memory alloy such as nickel-titanium alloys known in the art to have such properties. Wire 34 can then be preformed to the desired shape, can be compressed into a substantially straight configuration to pass through lumen 14, and will resume its desired shape once inside volume 30 where wire 34 will be free from steric constraints imposed inside the lumen 14. The resulting asymmetric isodose curve 40 can be further tailored by using solid radioactive particles 36 having differing specific activities to achieve the desired dosing.

In one embodiment, volume 30 and barrier 32 act to separate target tissue from the radiation source 24. Ideally, radiation therapy should make use of the inherent difference in radiosensitivity between the tumor and the adjacent normal tissues to destroy cancerous tissue while causing minimal disruption to surrounding normal tissues. At high doses of radiation, however, the percentage of exposed cells that survive treatment decreases with first-order kinetics in proportion to increasing radiation dose. With increasing cell death comes increasing risk of necrosis or tissue death in healthy tissue that is treated with a high dose of radiation. Accordingly, it is desirable to keep the maximum radiation dose delivered by the brachytherapy apparatus as low as possible while still delivering the desired therapeutic dose to the desired range of tissue. One method for achieving this result is to provide a "hotter" radiation source in a spaced apart relationship to the target tissue. In this way, because the intensity of the radiation emitted by a source drops with the square of the distance from the source, the effective dosage may be maintained below necrosis levels in target tissue closest to the interstitial brachytherapy apparatus while providing the required dosage to a greater depth into the target tissue. (See, e.g., U.S. Pat. No. 5,913,813 which is hereby incorporated by reference in its entirety.) The capability of the apparatus of the invention to deliver absorbed doses deeper into the target tissue than prior interstitial brachytherapy devices while controlling the dose in proximity to the apparatus to reduce or eliminate the risk of healthy tissue necrosis allows for the use of brachytherapy in a greater number of cases.

For example, it is desirable to provide an interstitial brachytherapy device configured to provide a dose in a

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therapeutic range, say between 40 to 60 Gray, at a distance between 0.5 and 1.0 cm from the outer spatial volume for an outer spatial volume having a diameter of 4.0 cm and being in contact with the resection cavity wall. In a typical embodiment, the radioactive source material ranges from approximately 150 to 450 mCi in activity and encompasses most of the target treatment area with a 0.4 to 0.6 Gray/hour isodose contour. At this treatment rate, treatment may be completed in approximately 3 to 7 days, or more commonly, in approximately 3 to 5 days.

In some applications, the desired dosing profile is consistent with the shape of the outer volume 30. That is, the absorbed dose within the target tissue at points equidistant from the surface 32 of the outer spatial volume 30 should be substantially uniform in substantially every direction. Put another way, the three dimensional isodose profiles generated by the radiation source should be substantially similar in shape to the outer spatial volume 30. Where the apparatus of the invention is deployed in soft tissue, it may also be important for the surface 32 of the outer spatial volume 30 to be sufficiently firm so as to force the target tissue to take on the shape of the surface 30 so that the desired relationship between the isodose profiles and the target tissue is achieved.

While the interstitial brachytherapy device 10 of FIG. 1 may employ these techniques to positive effect, this device specifically alters the isodose profile for applications where particularly sensitive tissue or other concerns result in a desire to limit the dosage on one or more sides of the device as illustrated by isodose curve 40.

In a further embodiment of the brachytherapy device 50 of the invention, illustrated in FIG. 3, three solid radiation particles 52 are provided in a linear portion 54 of radiation source 56, while two additional radiation particles 52 are provided on co-planar extending portions 58, 60 of radiation source 56. An end view of the device 50 of FIG. 3 is shown in FIG. 3A with extending portions 58, 60 provided in a single plane 62, and resulting in isodose profile 64. A second inner, expandable surface 66 can also be provided within outer surface 68; the inner surface 66 enclosing the entirety of radiation source 56.

By providing extending portions 58, 60 having radioactive particles in the indicated co-planar relationship, areas of reduced dosage can be created on opposed sides of the device while maintaining symmetric dosing in all other directions. Of course, the number of sources and their configuration can be changed to create a desired asymmetric dosage. For example, an additional source could be added, for example above plane 62, to result in a symmetric isodose profile in all directions except the direction below the plane 62 which would have a lower dosage.

An additional device 80 of the invention, shown in FIG. 4, includes a radiation source 82 that is made up of three wires 84, 86, 88, each having a plurality of solid radiation particles. Wire 86 is a straight wire extending along the longitudinal axis 90 of the device, while wires 84, 88 each curve as wire 34 described above with respect to FIG. 1. Wires 84, 88 are coplanar, resulting in an isodose profile 92 that is similar to isodose profile 64 of FIG. 3A. That is, the isodose profile will be symmetric in the plane in which the wires 84, 88 are disposed, but will have areas of reduced dosage in directions transverse to that plane (i.e., in FIG. 4, in the directions into and out of the page). As with the device 50 of FIGS. 3 and 3A, device 80 can be configured with more or fewer wires 84, 86, 88, and can be provided in configurations other than the depicted co-planar configuration in order to achieve desired asymmetric isodose profiles.

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The asymmetric dosing effect achieved by the devices described above can also be achieved using a liquid radiation source. For example, device 100, illustrated in FIG. 5, has an outer surface 102 defining an outer volume 104 and an inner surface 106 defining an inner volume 108. The inner surface 106 is asymmetrically shaped or located with respect to the longitudinal axis 110 of the device 100 so as to result in the desired asymmetric dosing when the inner volume 108 is filled with a radioactive fluid. The inner volume 108 is spaced apart from the outer surface 102 and can be filled with a material containing a predetermined radionuclide, for example, I-125, I-131, Yb-169 or other source of radiation, such as radionuclides that emit photons, beta particles, gamma radiation, or other therapeutic rays. The radioactive material contained within the inner volume 108 can be a fluid made from any solution of radionuclide(s), e.g., a solution of Ir-192, I-125 or I-131. A radioactive fluid can also be produced using a slurry of a suitable fluid containing small particles of solid radionuclides, such as Au-198, Y-90. Moreover, the radionuclide(s) can be embodied in a gel. One radioactive material useful in the invention is lotrex™, a sterile single use, non-pyrogenic solution containing sodium 3-(¹²⁵I)iodo-4-hydroxybenzenesulfonate (¹²⁵I-HIBS), available from Proxima Therapeutics, Inc. of Alpharetta, Ga. The inner volume 108 may be filled with radioactive fluid through port 112. Similarly, outer volume 104 can be filled on inflated using port 114.

A desired asymmetric dosing profile having the dosing characteristics described above may also be created by using asymmetric shielding between the radiation source and the target tissue as illustrated in FIGS. 6 through 9. In the device 120 of FIG. 6, a balloon 122 is located on the distal end of catheter 124. Radioactive particles 126 are disposed along the longitudinal axis 128 of the device. A portion of the surface, either inner or outer, of balloon 122 is coated with a radiopaque material 130 to result in asymmetric isodose curve 132. Radiopaque materials suitable for coating onto a polymeric surface of balloon 122 include, for example, barium, tungsten, bismuth, tantalum and tin.

A further device 140 having radiopaque shielding 142 is illustrated in FIG. 7. Device 140 includes an outer volume surface 144 and an inner volume surface 146. Inner surface 146 may contain a liquid radiation source, or may enclose one or more solid particles as used in device 120 (FIG. 6). In device 140, the radiopaque material 142 is coated onto a portion of either the inner or outer side of the inner volume surface 146, resulting in a desired asymmetric isodose profile 148.

Additional devices 160, 180 of the invention having radiation shielding 162 are illustrated in FIGS. 8 and 9, respectively. In these devices 160, 180, one or more radiation shields 162 are provided between and spaced apart from a radiation source (not shown) located along a longitudinal axis 164 of the device and the target tissue, which will be located outside of expandable surface 166. The radiation source can include a liquid or a solid radiation source as described above. Shields 162 can be formed from radiopaque materials including those described above with respect to the radiopaque coating and can extend longitudinally from a base on the device located within the expandable surface 166.

As shown in FIG. 8, device 160 has two radiation shields 162 on opposed sides of catheter 168. This configuration results in lower radiation dosing on the two sides of the device 160 on which the shields 162 are located as shown by isodose curve 170. Device 180 (FIG. 9) has a single radiation shield 162 resulting in an asymmetric isodose curve 182

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as shown. A person of ordinary skill in the art will recognize that other configurations may be employed to achieve desired isodose curves.

The interstitial brachytherapy apparatus of the invention can be used in the treatment of a variety of malignant tumors, and is especially useful for in the treatment of brain and breast tumors.

Many breast cancer patients are candidates for breast conservation surgery, also known as lumpectomy, a procedure that is generally performed on early stage, smaller tumors. Breast conservation surgery is typically followed by postoperative radiation therapy. Studies report that 80% of breast cancer recurrences after conservation surgery occur near the original tumor site, strongly suggesting that a tumor bed "boost" of local radiation to administer a strong direct dose may be effective in killing any remaining cancer and preventing recurrence at the original site. The apparatus described herein can be used for either the primary or boost therapy. Numerous studies and clinical trials have established equivalence of survival for appropriate patients treated with conservation surgery plus radiation therapy compared to mastectomy.

Surgery and radiation therapy are also the standard treatments for malignant solid brain tumors. The goal of surgery is to remove as much of the tumor as possible without damaging vital brain tissue. The ability to remove the entire malignant tumor is limited by its tendency to infiltrate adjacent normal tissue. Partial removal reduces the amount of tumor to be treated by radiation therapy and, under some circumstances, helps to relieve symptoms by reducing pressure on the brain.

A method according to the invention for treating these and other malignancies begins by surgical resection of a tumor site to remove at least a portion of the cancerous tumor and create a resection cavity. Following tumor resection, but prior to closing the surgical site, the surgeon intra-operatively places an interstitial brachytherapy catheter apparatus, having an inner spatial volume and an outer spatial volume as described above but without having the radioactive source material loaded, into the tumor resection cavity. Once the patient has sufficiently recovered from the surgery, the interstitial brachytherapy catheter is loaded with a radiation source. The radioactive source dwells in the catheter until the prescribed dose of radiotherapy is delivered, typically for approximately a week or less. The radiation source is then retrieved and the catheter is removed. The radiation treatment may end upon removal of the brachytherapy apparatus, or the brachytherapy may be supplemented by further doses of radiation supplied externally.

It will be understood that the foregoing is only illustrative of the principles of the invention, and that various modifications can be made by those skilled in the art without departing from the scope and spirit of the invention, including, but not limited to, combinations of elements from different embodiments found herein. All references cited herein are expressly incorporated by reference in their entirety.

What is claimed is:

1. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:
 - an expandable outer surface defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

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- a radiation source disposed completely within the expandable outer surface and located so as to be spaced apart from the apparatus volume, the radiation source further being asymmetrically located and arranged within the expandable surface to provide predetermined asymmetric isodose curves with respect to the apparatus volume.
2. A surgical apparatus for providing radiation treatment to target tissue comprising:
- an expandable outer surface defining an apparatus volume;
 - a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of solid radiation sources being provided in a spaced apart relationship on a single elongate member, the single elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources with respect to a longitudinal axis through the apparatus volume.
3. The apparatus of claim 2, further comprising a catheter in communication with the apparatus volume, the elongate member extending through the catheter into the apparatus volume.
4. The apparatus of claim 3, wherein the elongate member is formed of a shape memory alloy, the elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources, taking on a substantially straight shape while being inserted through the catheter to the apparatus volume, and resuming an asymmetric shape when extended into the apparatus volume.
5. A surgical apparatus for providing radiation treatment to target tissue comprising:
- an expandable outer surface defining an apparatus volume;
 - a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, wherein at least one of the plurality of solid radiation sources has a different specific activity from at least one other solid radiation source.
6. A surgical apparatus for providing radiation treatment to target tissue comprising:
- an expandable outer surface defining an apparatus volume;
 - a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising

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- ing a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of radiation sources being provided on at least two elongate members extending into the apparatus volume, at least one of the elongate members being shaped to provide asymmetric placement of a radiation source with respect to a longitudinal axis through the apparatus volume.
7. The apparatus of claim 6, wherein each of the at least two elongate members includes a plurality of solid radiation sources provided in a spaced apart relationship.
8. The apparatus of claim 1, wherein the expandable outer surface is sufficiently rigid to deform the target tissue into the shape of the expandable outer surface, causing the predetermined asymmetric isodose curves to penetrate into the target tissue to a prescribed depth.
9. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:
- an expandable outer surface having a base and defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;
 - a radiation source disposed completely within and spaced apart from the expandable outer surface; and
 - an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves with respect to the apparatus volume.
10. The apparatus of claim 9, wherein the asymmetric radiation shield comprises a radio-opaque material disposed on only a portion of the expandable outer surface.
11. The apparatus of claim 10, wherein the expandable outer surface comprises an inflatable balloon.
12. The apparatus of claim 11, wherein the radiation shield comprises a barium material disposed a portion of the inflatable balloon.
13. The apparatus of claim 9, further comprising at least one radiation shield extending from the base of the expandable outer surface toward an opposite end of the expandable surface, the shield being in between and spaced apart from the radiation source and the expandable outer surface, the shield forming a radio-opaque barrier between a portion of the radiation source and the target tissue.
14. The apparatus of claim 13, wherein the radiation shield comprises two shields provided on opposite sides of the radiation source.

* * * * *

Exhibit 4

United States District Court
For the Northern District of California

E-FILED on 4/27/07

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

XOFT, INC.,

Plaintiff,

v.

CYTYC CORPORATION; and PROXIMA
THERAPEUTICS, INC.,

Defendants.

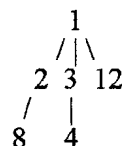
No. C-05-05312 RMW

CLAIM CONSTRUCTION ORDER

[Re Docket Nos. 48, 50, 53]

Xoft, Inc. sued Cytyc Corporation and one of its subsidiaries, Cytyc Surgical Products II, Inc., (collectively "Cytyc") for a declaratory judgment of non-infringement and invalidity of U.S. Patent Nos. 5,913,813 and 6,413,204. Cytyc responded by filing counterclaims for infringement of the same patents and currently asserts that Xoft infringes six claims of the '813 patent¹ and twenty

¹ Cytyc asserts claims 1, 2, 3, 4, 8, and 12. Claim 1 is an apparatus claim and the only independent claim of the '813 patent. Claims 2, 3, and 12 depend directly from claim 1. Claim 4 depends from claim 3, and claim 8 depends from claim 2. The following is a graphic representation of the relationship of the asserted claims:

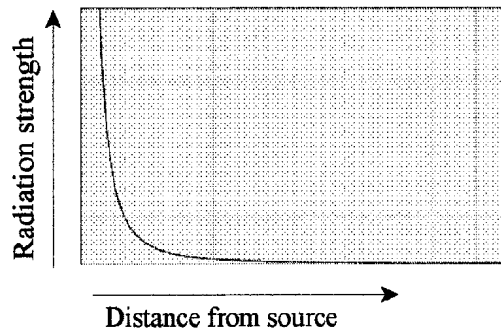


CLAIM CONSTRUCTION ORDER—No. C-05-05312 RMW
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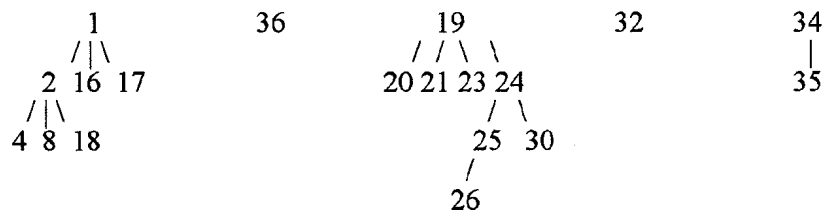
claims of the '204 patent². The application for the '204 patent was filed as a continuation-in-part of the '813 patent; the former purports to incorporate by reference the latter. '204 patent, col. 1, ll. 10-11. The parties seek construction of eight terms or phrases from the '813 patent and twenty-one terms or phrases from the '204 patent.

I. BACKGROUND

The patents-in-suit are directed to methods and apparatus for treatment of proliferative tissue diseases. The prior art discloses that a radiation source can be implanted at a tumor site to irradiate any remaining diseased tissue; this process is known as interstitial brachytherapy. The parties agree that for the purposes of this suit, the strength of radiation may be assumed to decrease with the square of the distance from the radiation source. The graph of the equation $y = 1/x^2$ thus can be used as an approximation of the relationship between the radiation strength and distance. The graph, shown below, illustrates that the radiation strength close to the radiation source is disproportionately higher than that at a relatively small distance away from the radiation source.

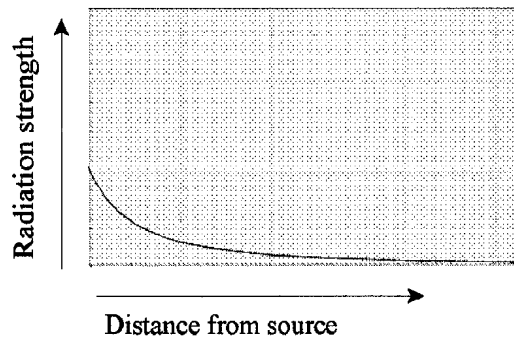


² Cytoc asserts claims 1, 2, 3, 4, 8, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26, 30, 32, 34, 35, and 36 of the '204 patent. Claims 1 and 36 are the only independent apparatus claims. From claim 1 depend claims 2, 16, and 17. From claim 2 depend claims 4, 8, and 18. Claims 19, 32, and 34 are independent method claims. Claims 20, 21, 23, and 24 all depend from claim 19. Claim 25 depends from claim 24, and claim 26 depends from claim 25. Claim 30 also depends from claim 24. Claim 35 depends from claim 34. The following is a graphic representation of the relationship of the asserted claims:



This shows one of the problems encountered in radiation therapy, namely, that tissue close to the radiation source may get more radiation than a physician would prefer. When using interstitial therapy, a physician may wish to give all tissue within a certain distance—say, for example, 3 centimeters—from the tumor site a certain dose of radiation. However, tissue closer to the tumor site—say, 1 centimeter—will receive a much higher dose of radiation because of the inverse-square relationship. This means that healthy tissue near the tumor site may be killed by the radiation, which is an undesirable result.

Following the teachings of the patents-in-suit, the very high levels of radiation near the source can be avoided by simple mechanical means. Surrounding the radiation source on all sides with empty space (or some material other than living tissue) prevents the highest levels of radiation from affecting living tissue, giving the tissue a radiation dose profile that looks something like this:



II. ANALYSIS

A. Terms of the '813 patent

"Inner spatial volume"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
A region of space surrounded by an outer spatial volume that is defined by a closed inflatable chamber	Inner balloon in two-balloon device or spherical solid radionuclide in one-balloon device

The summary of the invention provides that

it is possible to deliver a desired radiation dose at a predetermined radial distance from a source of radioactivity by providing a first spacial³ volume at the distal end of a catheter and a second spatial volume defined by a surrounding of the first spatial

³ Presumably all occurrences of "spacial" in the '813 patent should be read as "spatial."

1 volume by a polymeric film wall where the distance from the spatial volume⁴ and
2 the wall is maintained substantially constant over their entire surfaces. One of the
3 inner and outer volumes is filled with either a fluid or a solid containing a
4 radionuclide(s) while the other of the two volumes is made to contain either a low
5 radiation absorbing material, e.g., air or even a more absorptive material, such as an

6 surrounding radiation absorbing material serves to control the radial profile of the
7 radioactive emissions from the particular one of the inner and outer volumes
8 containing the radionuclide(s) so as to provide a more radially uniform radiation
9 dosage in a predetermined volume surrounding the outer chamber. Where the core
10 contains the absorbent material, the radial depth of penetration of the radiation can be
11 tailored by controlling the core size.

12 '813 patent, col. 1, l. 50-col. 2, l. 3. The first two claims of the '813 patent read:

13 1. Apparatus for delivering radioactive emissions to a body location with a uniform
14 radiation profile, comprising:

15 (a) a catheter body member having a proximal end and distal end;

16 (b) an inner spatial volume disposed proximate the distal end of the catheter
17 body member;

18 (c) an outer, closed, inflatable, chamber defined by a radiation transparent
19 wall affixed to the body member proximate the distal end thereof in
20 surrounding relation to the inner spatial volume with a predetermined constant
21 spacing between said inner spatial volume and the radiation transparent wall;

22 (d) a material containing a radionuclide(s) disposed in one of the inner spatial
23 volume and outer chamber; and

24 (e) means disposed in the other of the inner spatial volume and outer chamber
25 for rendering uniform the radial absorbed dose profile of the emissions from
26 the one of the inner spatial volume and outer chamber containing the
27 radionuclides.

28 2. The apparatus as in claim 1 wherein said inner spatial volume is an inner closed,
chamber defined by a further radiation transparent wall.

'813 patent, col. 4, ll. 32-54. Since all claims of this patent other than claim 1,
construction of "inner spatial volume" is critical.

In most embodiments of the invention disclosed in the patent specification, the inner spatial
volume is a region of space surrounded by an outer spatial volume that is defined by a closed
inflatable chamber. See '813 patent, col. 2, ll. 44-63; col. 3, ll. 9-16, 42-48; col. 4, ll. 16-20; figs. 1,

⁴ Presumably this "spatial volume" should be taken to be the first spatial volume, which would mean
that the polymeric film wall forms the outer boundary of the second spatial volume and that the second
spatial volume is of a uniform thickness on all sides of the first spatial volume. Such a reading would
comport with claim 1(c).

3-5. However, the patentee drafted the claims in such a way as to make clear that the inner spatial volume was not necessarily so limited:

Those skilled in the art will appreciate that instead of having the inner spatial volume 30 defined by a generally spherical polymeric film wall as at 32, the catheter body member 12 may have a solid spherical radiation emitting material in which event that solid sphere would be surrounded with the outer spherical wall 36 with the spatial volume therebetween occupied by a radioactive ray absorbent material, such as air, water or a contrast material.

'813 patent, col. 2, ll. 55-63.

Although somewhat awkwardly worded, the language of the patent allows for the inner volume to be defined by something other than a region enclosed by a polymeric wall. As Cytyc points out, Xoft's construction conflates the boundary of the volume with the volume itself. Cytyc's proposed construction, however, is a paraphrasing of the language of claim 1 that only clarifies a little the language of the patent. Furthermore, Cytyc's proposed construction would exclude an inner volume defined by a solid sphere, and thus cannot be correct.

Xoft objects that an abstract concept like a region of space cannot be part of an apparatus. Xoft is correct. However, the language of the patent does not imply that the inner volume is ever defined by something other than a physical object. In all embodiments of the invention disclosed in the '813 patent, the boundary of the inner volume is either a polymeric film wall or the edge of a solid sphere. Furthermore, it would seem difficult to fill one volume with radioactive liquid and the other with another fluid if the two volumes were not separated by some structure (which would necessarily be the outer boundary of the inner spatial volume.) See '813 patent, col. 1, ll. 57-62. The patent is even entitled "Double-Wall Balloon Catheter for Treatment of Proliferative Tissue." Xoft's expert, Dr. Lovoi, acknowledged that an "inner spatial volume" is a volume that is inside another volume. Lovoi Dep. at 101:25-102:7. The court defines "inner spatial volume" as "a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the edge of a solid radionuclide sphere."

<i>Claim Language</i>	<i>Court's Construction</i>
"inner spatial volume"	a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere

"Outer, closed, inflatable chamber"

<i>Cytec's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	Inflatable balloon, i.e., deflated balloon

Part (c) of claim 1 explains that the "outer, closed, inflatable chamber" is "defined by a radiation transparent wall affixed to the body member proximate the distal end thereof in surrounding relation to the inner spatial volume with a predetermined constant spacing between said inner spatial volume and the radiation transparent wall." '813 patent, col. 4, ll. 40-45. The preferred embodiment recites a similar structure: "Surrounding the spatial volume 30 is an outer chamber 34 defined by an outer polymeric film wall 36 that is appropriately spaced from the wall 32 of the inner chamber 30 when the two chambers are inflated or otherwise filled and supported." '813 patent, col. 2, ll. 37-41. There is no support in the patent for Xoft's argument that "outer, closed, inflatable chamber" should be limited to only a balloon in a deflated state. The court will therefore adopt Cytec's proposal and not otherwise define this term.

<i>Claim Language</i>	<i>Court's Construction</i>
"outer, closed, inflatable chamber"	outer, closed, inflatable chamber

"Predetermined constant spacing"

<i>Cytec's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

"Predetermined constant spacing between said inner spatial volume and radiation transparent wall"

<i>Cytec's proposed construction</i>	<i>Xoft's proposed construction</i>
The spacing between the inner spatial volume and the radiation transparent wall of the outer, closed, inflatable chamber, when inflated, can be made constant in all directions if the outer chamber is spherical, or constant along a radial plane if the outer chamber is not spherical	(indefinite)

Xoft argues that the '813 patent is indefinite because it does not disclose how one "predetermines" the amount of spacing. Xoft points out that the spacing between the edges of the inner and outer volumes may change as parts of the apparatus are inflated or deflated, so the spacing is not constant. Cytec's expert explained that "predetermined constant spacing" means that "the

spacing between the inner spatial volume and the wall of the outer inflatable chamber can be made constant in all directions if the outer chamber is spherical, or constant along a radial direction if non-spherical, whenever the outer chamber is inflated." Su Decl. (dkt. # 49), Ex. D (Verhey Decl.) at 7 (citations omitted). Cytyc also argues that "[o]ne skilled in the art knows how to determine an appropriate 'predetermined constant spacing' and Xoft provides no evidence, testimony, or case law to the contrary. Xoft cannot possibly show that the term is indefinite by clear and convincing evidence." Reply Br. (dkt. # 53) at 15.

Because 35 U.S.C. § 282 gives a patent "a statutory presumption of validity," a challenger bears the burden of proving "by clear and convincing evidence" that a patent is invalid. *Monsanto Co. v. Scruggs*, 459 F.3d 1328, 1336-37 (Fed. Cir. 2006). "[P]atent documents need not include subject matter that is known in the field of the invention." *S3 Inc. v. NVIDIA Corp.*, 259 F.3d 1364, 1371 (Fed. Cir. 2001). From the testimony of Dr. Verhey, it appears that one skilled in the art would know how to "predetermine" the amount of spacing.⁵ See Tr. at 56-61, 85-89. Xoft offered no evidence suggesting otherwise. As the burden of proof is Xoft's, its indefiniteness argument necessarily fails given the absence of supporting evidence. The court will therefore adopt Cytyc's proposed construction of "predetermined constant spacing between said inner spatial volume and radiation transparent wall" modified only to make the definition easier to understand. A separate construction for "predetermined constant spacing" is not necessary.

Claim Language	Court's Construction
"predetermined constant spacing"	(no construction necessary)
"predetermined constant spacing between said inner spatial volume and radiation transparent wall"	spacing predetermined by one skilled in the art between the wall or edge of the inner spatial volume and the radiation transparent wall of the outer, closed, inflatable chamber, when inflated, which is constant in all directions if the outer chamber is spherical, or constant along a radial plane if the outer chamber is not spherical

⁵ Xoft argues that the size of the cavity determines the size of the apparatus when fully inflated, but this alone does not determine the spacing between the inner spatial volume and the wall of the outer chamber.

1 **"Rendering uniform"**

2

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	Making the same, i.e., causing to have the same value or characteristic at all points.

3

4 **"Means . . . for rendering uniform the radial absorbed dose profile of the emissions"**

5

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
Function: Modifying the ratio of the absorbed dose at a depth of interest in the target tissue to the absorbed dose at the surface of the tissue.	Function: Making the dose along a radius extending from the radionuclide outwardly from the outer chamber wall the same at every point on the radius.
Structure: A radiation absorbing or attenuating material, e.g., air, x-ray contrast fluid, contrast media used in angiography, water, a gas, or barium sulfate.	Structure: No such means disclosed in '813 patent, means for making more uniform disclosed as substance within outer chamber.

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11 Xoft's argument is that "uniform" must be taken literally, and the apparatus must produce
12 radiation that does not decrease in strength with increasing distance from the source.⁶ The parties do
13 not dispute that Xoft's construction would require a physical impossibility; the strength of radiation
14 necessarily decreases with distance from its source. Xoft, however, seeks to interpret "uniform" in a
15 vacuum. The meaning of a particular word in a claim must be interpreted in light of the rest of the
16 patent. *Ekchian v. Home Depot, Inc.*, 104 F.3d 1299, 1303 (Fed. Cir. 1997).

17 While the patent could have been drafted with more clarity, it is readily apparent that the
18 patentee did not contemplate absolute uniformity. Figure 4 of the patent (reproduced below) is a
19 comparison between the distance versus radiation dose plots of two scenarios. Line 40 shows the
20 radiation dose that would result if chamber 36 were filled with a radioactive fluid. '813 patent, col.
21 3, ll. 20-24. Line 42 shows the radiation dose that would result if, following the teachings of the
22 patent, the same radioactive fluid were contained only in chamber 32. '813 patent, col. 3, ll. 24-28.
23 As explained in the patent, "Comparing the plots 40 and 42, by providing the concentric
24 arrangement depicted, the absorbed dose profile in the space between the 2 cm site and the wall of
25 the outer balloon is maintained much more uniform, thus preventing over-treatment of body tissue at
26

27

28 ⁶ Xoft also stated that it would "submit a Motion for Summary Judgment on this issue prior to the conduct of the *Markman* hearing," Responsive Br. (dkt. # 50) at 14, but did not do so.

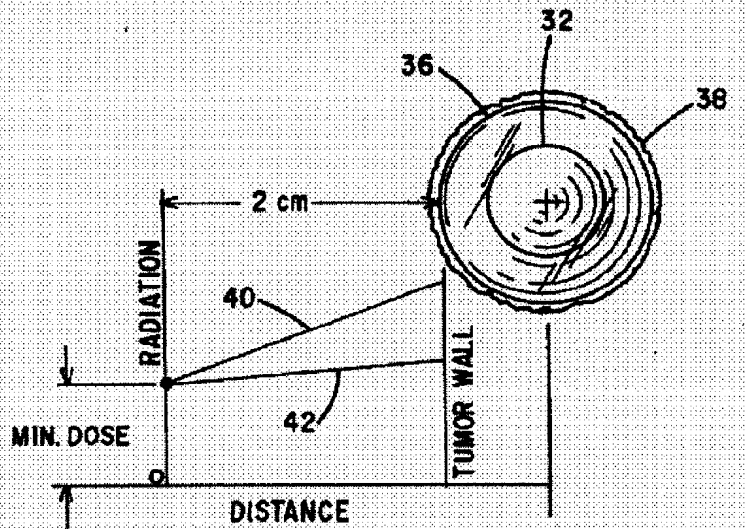
1 or close to the outer wall 36 of the
2 instrument." '813 patent, col. 3, ll.
3 28-33.

4 The patentee obviously did
5 not expect absolute uniformity of
6 radiation dosing. To interpret
7 "uniform" in the manner urged by
8 Xoft would go against the clear
9 intent of the patentee. In *Bausch &*
10 *Lomb, Inc. v. Barnes-*

11 *Hind/Hydrocurve, Inc.*, 796 F.2d

12 443 (Fed. Cir. 1986), the defendant made a similar argument regarding the patentee's use of the term
13 "smooth" with respect to the edges of contact lenses. The Federal Circuit looked to the intrinsic
14 evidence and found that "smooth" did not mean absolutely ridge free but rather that it meant
15 "smooth enough to serve the inventor's purposes, *i.e.*, not to inflame or irritate the eyelid of the
16 wearer or be perceived by him at all when in place." *Id.* at 450. In this case, the inventor's purpose
17 was to deliver radiation more uniformly than had previously been done, "thus preventing over-
18 treatment of body tissue at or close to the outer wall . . . of the instrument." '813 patent, col. 3, ll.
19 28-32. The court will therefore define "rendering uniform" to mean to make the absorbed dose of
20 radiation more uniform in order to prevent over-treatment of body tissue at or close to the outer wall
21 of the instrument.

22 Since limitation language "means . . . for rendering uniform the radial absorbed dose profile
23 of the emissions" is in means-plus-function format, the function must be construed and the
24 corresponding structure or its equivalent identified in the specification. *BBA Nonwovens*
25 *Simpsonville, Inc. v. Superior Nonwovens, L.C.C.*, 303 F.3d 1332, 1343 (Fed. Cir. 2002). As
26 discussed, Xoft's definition of the function requires absolute uniformity which is not possible and
27 which is not what the patent requires or the inventor intended. Cytoc's proposed definition construes
28 the function as "modifying the ratio of the absorbed dose at a depth of interest in the target tissue to



the absorbed dose at the surface tissue." Although this appears to be a function of the invention, Cytec's definition is too broad because it encompasses absorbed doses at the surface tissue that are not substantially uniform to absorbed doses at the target tissue. In other words, Cytec's definition would not only encompass the radiation dose profile of line 42 above, but would also encompass the radiation dose profile of line 40. Furthermore, all radiation dose profiles between line 40 and line 42 that result in over-treatment of the surface tissue would also be included under Cytec's definition. A more accurate construction of the function would require the absorbed dose at the target tissue and the absorbed dose at the surface tissue to be more uniform to prevent over-treatment of the surface tissue. Thus, the court defines the function of the "means . . . for rendering uniform the radial absorbed dose profile of the emissions" as making the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument.

Cytec also identifies a radiation-absorbing or -attenuating material as the corresponding structure. At the claim construction hearing, Xoht argued that the uniformity of the radiation dose curve is solely affected by distance from the radiation source; the parties agree that this is true. *See* Tr. at 60-61. Although the composition of the material is not critical to the function, the radiation-absorbing or -attenuating material provides the distance necessary for achieving the uniformity in radiation dose curve. Thus, the court construes the language consistently with Cytec's position.

<i>Claim Language</i>	<i>Court's Construction</i>
"rendering uniform"	to make the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument
"Means . . . for rendering uniform the radial absorbed dose profile of the emissions"	<p>Function: Making the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument.</p> <p>Structure: A radiation absorbing or attenuating material, <i>e.g.</i>, air, x-ray contrast fluid, contrast media used in angiography, water, a gas, or barium sulfate or their equivalents.</p>

"The radioactive material"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
The material of claim 1 containing a radionuclide.	(indefinite)

Claim 8 of the patent covers "[t]he apparatus as in claim 2 wherein the inner chamber contains the radioactive material." Claim 2 depends from claim 1. The parties dispute whether "a material containing a radionuclide(s)" suffices as an antecedent basis for "the radioactive material." It is readily apparent that the "radioactive material" in claim 8 refers back to "a material containing a radionuclide" described in claim 1, since "radionuclide" is the only radioactive material mentioned in claim 1. Anyone skilled in the art would so conclude. Xoft's contention that the term "radioactive material" is indefinite because it contains no antecedent basis is without merit. Xoft offers no authority suggesting that the antecedent basis of a term used in a dependent claim must be stated in identical words.⁷ The court, therefore construes "the radioactive material" in claim 8 to be the "radionuclide(s)" referred to in claim 1.

<i>Claim Language</i>	<i>Court's Construction</i>
"The radioactive material"	The material of claim 1 containing a radionuclide.

"A plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
A plurality of radioactive solid particles placed at pre-determined locations within the inner spatial volume to provide a desired dose profile that is the sum of the radiation profiles of the plurality of particles.	Static array of solid radioactive particles each placed in a single location and mounted on distal ends of separate wires. Desired composite radiation profile" is indefinite.

Claim 12 of the patent is directed to "[t]he apparatus as in claim 1 wherein the material containing a radionuclide comprises a plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile." Xoft argues claim 12 is indefinite on two grounds: first, that "desired composite radiation profile" is not

⁷ At the *Markman* hearing, Xoft stated that it would provide a citation to such supporting authority. Tr. at 64. Xoft, however, has not done so.

defined, and second, that "inner spatial volume" is indefinite because no physical structure bounds it. The court rejects Xoft's second argument for the reasons given when construing "inner spatial volume" above. The court rejects Xoft's first argument because it presents no evidence that one skilled in the art would not understand "desired composite radiation profile."⁸ Cytyc's proposed construction does not clarify the meaning of claim 12. However, since the language is understandable as is, no construction of "a plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile" is necessary or appropriate.

<i>Claim Language</i>	<i>Court's Construction</i>
"A plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile"	(no construction needed)

B. Terms of the '204 patent

Claim 1 of the '204 patent is similar to claim 1 of the '813 patent. Claim 1 of the '204 patent describes:

An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:

- (a) a catheter body member having a proximal end and distal end;
- (b) an inner spatial volume disposed proximate to the distal end of the catheter body member;
- (c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
- (d) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

⁸ It would seem that for one skilled in the art, it would be a relatively simple matter to add up the individual radiation profiles of individual particles. *See* Tr. at 75-76.

"Interstitial"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	Site in natural or surgically created cavity in body.

"Brachytherapy"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
Radiation therapy delivered by a spatially confined radiation source at or near the site of the diseased tissue.	Radiation therapy delivered by a spatially confined radionuclide at or near a tumor or other proliferative tissue disease site.

"Interstitial brachytherapy"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
Brachytherapy applied directly to the interspaces of a body tissue, where the interspaces are not naturally occurring.	Radiation therapy delivered by a spatially confined radionuclide at or near a tumor site in a natural or surgically created cavity in a body.

Cytac argues that "interstitial" and "brachytherapy" should be constructed together; Xoft seeks a separate construction for each word. Cytac also complains that Xoft seeks to limit "brachytherapy" to radionuclides, arguing that the definition should encompass any radiation source. However, the patent provides a clear definition of "brachytherapy": "The term 'brachytherapy,' as used herein, refers to radiation therapy delivered by a spatially confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site." '204 patent, col. 1, ll. 30-33. Here, the patentee clearly acted as his own lexicographer, and Cytac's arguments for a broader definition do not acknowledge this clear definition. The court construes "brachytherapy" to mean "radiation therapy delivered by a spatially-confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site."⁹

Xoft argues that "interstitial" means any body cavity, while Cytac argues that "interstitial" should be limited to only non-naturally-occurring cavities. As Xoft points out, one medical dictionary defines "interstitial" as "1. Placed or lying between. 2. Pert. to

⁹ This definition does not resolve the parties' dispute over whether "radioactive material" should be read to encompass only "radionuclides" (as Xoft wishes) or any "radiation source" (as Cytac urges). As the parties have separately sought construction of "radioactive material," the court will address construction of that phrase below.

1 interstices or spaces within an organ or tissue." TABER'S CYCLOPEDIA MEDICAL
2 DICTIONARY, 1007 (Clayton M. Thomas, ed., 17th ed. 1993). Although not cited by the
3 parties, a British oncology text indicates that "interstitial" has a particular meaning in the
4 field of the invention:

5 Two main techniques are used for the delivery of radiation which is given
6 either as an external beam or as short range radiation from an implanted radioactive
7 source. External beam radiation usually involves megavoltage produced by linear
8 accelerator as photons or electrons or from cobalt sources in the form of relative low
9 energy X-rays or gamma rays. The latter are often used to treat relatively superficial
10 lesions such as basal cell carcinoma or recurrences within the skin. High energy
11 radiation can be used to treat deeply located lesions such as prostatic carcinomas
without delivering an excessive dose to adjacent normal tissue. . . .

12 Interstitial implant irradiation gives a high local dose to the tumour and
usually employs sources such as radium, iridium, or caesium used in the form of
13 needles or wires implanted in the tumour. This technique is widely used in the
treatment of head and neck cancers to deliver a high tumour dose without irradiation
14 to sensitive organs such as the lens of the eye or the spinal cord.

15 I.S. Fentiman, *The local Treatment of Cancer*, INTRODUCTION TO THE CELLULAR & MOLECULAR
16 BIOLOGY OF CANCER, 434, 446 (L.M. Franks & N.M. Teich, eds., 2d ed. 1991).

17 However, Cytac points out that regardless of any generally-accepted meaning of "interstitial"
18 in the field of the invention, the patentee limited "interstitial" during prosecution to refer to only
19 surgically-created cavities (and similarly defined "intercavitary" to refer to natural body cavities):

20 Turning to the cited prior art, the Ishiwara device comprises a
thermotherapeutic apparatus having a catheter body member, an inner lumen
21 surrounded by an outer lumen, and a radiation source contained within the inner
22 lumen. . . . Ishiwara's apparatus is inserted into a body cavity. Hence, the apparatus
23 does not provide *interstitial* radiation treatment, as Applicant's invention requires, but
24 rather intercavitary radiation treatment.

25 Su Decl. (dkt. # 49), Ex. C (Amendment & Resp.) at 11 (citations omitted). This is consistent with
26 the background section of the patent, which mentions surgical cavities several times but not natural
27 ones. '204 patent, col. 1, ll. 19, 23, 25, 63, col. 2, l. 1. Also, although the summary section does not
28 specify what type of cavities the apparatus claims are directed to, the summary makes clear that the
method claims are directed to a method that "includes surgically creating access to the proliferating
tissue within a patient and surgically resecting at least a portion of the proliferating tissue to create a
resection cavity within body tissue." *Id.*, col. 3, ll. 3-6.

1 The parties did not brief the issue of how much weight the court should afford the
2 prosecution history in this instance.¹⁰ The Federal Circuit has instructed that "[a]lthough prosecution
3 history can be a useful tool for interpreting claim terms, it cannot be used to limit the scope of a
4 claim unless the applicant took a position before the PTO that would lead a competitor to believe
5 that the applicant had disavowed coverage of the relevant subject matter." *Schwing GmbH v.*
6 *Putzmeister Aktiengesellschaft*, 305 F.3d 1318, 1324 (Fed. Cir. 2002). Here, the patentee clearly
7 disavowed coverage of intercavitary radiation treatment when arguing to the PTO. Given the

13 ¹⁰ In its recent *en banc* explanation of the evidence to be used in construing claims, the Federal
14 Circuit devoted a paragraph to prosecution history:

15 In addition to consulting the specification, we have held that a court "should
16 also consider the patent's prosecution history, if it is in evidence." *Markman*, 52 F.3d
17 at 980; *see also Graham v. John Deere Co.*, 383 U.S. 1, 33, 86 S.Ct. 684, 15 L.Ed.2d
18 545 (1966) ("[A]n invention is construed not only in the light of the claims, but also
19 with reference to the file wrapper or prosecution history in the Patent Office."). The
20 prosecution history, which we have designated as part of the "intrinsic evidence,"
21 consists of the complete record of the proceedings before the PTO and includes the
22 prior art cited during the examination of the patent. *Autogiro*, 384 F.2d at 399. Like
23 the specification, the prosecution history provides evidence of how the PTO and the
24 inventor understood the patent. *See Lemelson v. Gen. Mills, Inc.*, 968 F.2d 1202,
25 1206 (Fed. Cir. 1992). Furthermore, like the specification, the prosecution history
26 was created by the patentee in attempting to explain and obtain the patent. Yet
27 because the prosecution history represents an ongoing negotiation between the PTO
28 and the applicant, rather than the final product of that negotiation, it often lacks the
clarity of the specification and thus is less useful for claim construction purposes.
See Inverness Med. Switz. GmbH v. Warner Lambert Co., 309 F.3d 1373, 1380-82
(Fed. Cir. 2002) (the ambiguity of the prosecution history made it less relevant to
claim construction); *Athletic Alternatives, Inc. v. Prince Mfg., Inc.*, 73 F.3d 1573,
1580 (Fed. Cir. 1996) (the ambiguity of the prosecution history made it "unhelpful as
an interpretive resource" for claim construction). Nonetheless, the prosecution
history can often inform the meaning of the claim language by demonstrating how the
inventor understood the invention and whether the inventor limited the invention in
the course of prosecution, making the claim scope narrower than it would otherwise
be. *Vitronics*, 90 F.3d at 1582-83; *see also Chimie v. PPG Indus., Inc.*, 402 F.3d
1371, 1384 (Fed. Cir. 2005) ("The purpose of consulting the prosecution history in
construing a claim is to 'exclude any interpretation that was disclaimed during
prosecution.'"), quoting *ZMI Corp. v. Cardiac Resuscitator Corp.*, 844 F.2d 1576,
1580 (Fed. Cir. 1988); *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576
(Fed. Cir. 1995).
Phillips v. AWH Corp., 415 F.3d 1303, 1317 (Fed. Cir. 2005) (*en banc*).

intrinsic evidence is of primary importance¹¹ and all supports Cytec's position, the court construes "interstitial" to mean "involving a surgically-created cavity in a body."

In light of the constructions of "interstitial" and "brachytherapy" above, no further construction of "interstitial brachytherapy" is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"interstitial"	involving a surgically-created cavity in a body
"brachytherapy"	radiation therapy delivered by a spatially-confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site
"interstitial brachytherapy"	(no construction necessary)

"Inner spatial volume"

<i>Cytec's proposed construction</i>	<i>Xoft's proposed construction</i>
A region of space surrounded by an outer spatial volume that is defined by an expandable surface element	Inner balloon in two-balloon device or spherical solid radionuclide in one-balloon device.

The phrase "inner spatial volume" appears in both patents-in-suit. The parties' arguments regarding the meaning of "inner spatial volume" are similar for each patent. The relevant portions of the specification are the same, and, additionally, the '204 patent purports to incorporate by reference the '813 patent. '204 patent, col. 1, ll. 10-11. The court will therefore construe "inner spatial volume" in the '204 patent in the same manner as for the '813 patent.

<i>Claim Language</i>	<i>Court's Construction</i>
"inner spatial volume"	a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere.

¹¹ The extrinsic evidence that Cytec used "intercavitary" in literature and advertising in a manner that encompasses the definitions of "interstitial" and "intercavitary" it advances now, *see* Tr. at 93, is of little weight in this situation. Similarly, evidence presented by Cytec that Xoft represented to the FDA that the term "interstitial" "is a more appropriate word for a cavity that is surgically created as compared to a natural body cavity," (*see* Decl. of Henry Su Supp. Cytec's Supplemental Claim Construction Br., Ex. A, is not entitled to significant weight although it does suggest that one skilled in the art construes the term as Cytec proposes.

"Outer spatial volume"

<i>Cytec's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required) <i>or</i> A region of space defined by an expandable surface element and surrounding an inner spatial volume.	Balloon or cage.

The phrase "outer spatial volume" in the '204 patent is analogous to the "outer, closed, inflatable chamber" of the '813 patent. The "outer spatial volume" is also explained in a similar manner; it is "defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume." '204 patent, col. 8, ll. 22-25. Xoft again confuses the concepts of a volume with the boundary of a volume. Cytec's proposed construction is congruent with the language of claim 1 of the '204 patent, so the court will construe "outer spatial volume" as "a region of space defined by an expandable surface element and surrounding an inner spatial volume."

<i>Claim Language</i>	<i>Court's Construction</i>
"outer spatial volume"	a region of space defined by an expandable surface element and surrounding an inner spatial volume

"Expandable surface element"

<i>Cytec's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required) <i>or</i> A device that can be expanded or inflated, such as an expandable cage or an inflatable balloon.	Deflated balloon or collapsed cage.

Xoft's basic argument is that "expandable surface element" must be a deflated structure because once something is fully inflated, it is no longer expandable. Xoft also points out that part (d) of claim 1 refers to the "isodose profile" being "substantially similar in shape to the expandable surface element" without specifying whether the expandable surface element is fully expanded. It is apparent that the patentee intended "expandable surface element" to refer to a structure whether it was fully inflated or not. Xoft's proposed construction would have this element wink out of

1 existence at full inflation, leaving the "outer spatial volume" unbounded and giving the "isodose
2 profile" no shape. The court agrees with Cytyc that no construction of the term is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"expandable surface element"	(no construction needed)

6 **"Radiation source"**

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	radionuclide

9 The patent provides a clear definition of "brachytherapy": "The term 'brachytherapy,' as used
10 herein, refers to radiation therapy delivered by a spatially confined radioactive material inserted into
11 the body at or near a tumor or other proliferative tissue disease site." All asserted independent
12 claims of the '204 patent contain the phrase "interstitial brachytherapy," which the court has
13 construed as "radiation therapy delivered by a spatially-confined radioactive material inserted into
14 the body at or near a tumor or other proliferative tissue disease site." Cytyc's argument that
15 "radiation source" should not be constructed to exclude any radiation sources must be rejected; the
16 claims clearly do not contemplate a radiation source other than "radioactive material."

17 There is still, however, the question of whether "radioactive material" means the same thing
18 as Xoft's proposed construction of "radionuclide."¹² In describing the preferred embodiment, the
19 patent says: "[t]he inner volume **30** is then filled with a material containing a predetermined
20 radionuclide, for example, I-125, I-131, Yb-169 *or other source of radiation, such as radionuclides*
21 *that emit photons, beta particles, gamma radiation, or other therapeutic rays.*" '204 patent, col. 4,
22 ll. 9-13 (emphasis added). Since all the examples of sources of radiation given in the specification
23 are radionuclides, the patentee appears to have intended to define "radioactive material" as
24 "radionuclides." Cytyc argued at the *Markman* hearing that "or other therapeutic rays" could refer to
25 other sources such as x-rays. The words "or other therapeutic rays," however, clearly refers to types
26
27
28

¹² The parties have agreed that "radionuclide" means "an isotope that undergoes radioactive decay."

of radionuclides. Cytyc's construction would require the patentee to have inserted the word "or" before "gamma radiation," indicating the end of the list of types of radionuclides.¹³

Dictionary definitions are consistent with construing "radiation source" as a "radionuclide." One definition of "radioactive" is "[a] descriptive term for a material made up of atoms in which radioactivity occurs." AMERICAN HERITAGE NEW DICTIONARY OF CULTURAL LITERACY (3d ed. 2006). A medical dictionary provided by Xoft defines "radioactive" as "giving off radiation as the result of the disintegration of the nucleus of an atom." MOSBY'S MEDICAL, NURSING, AND ALLIED HEALTH DICTIONARY, 1326 (Kenneth N. Anderson *et al.* eds., 4th ed. 1994). Cytyc has not presented evidence that one skilled in this art would understand "radioactive material" any differently. The court agrees with Xoft—the term "radioactive" in the context of the '204 patent does not encompass such radiation sources as x-ray tubes, and "radiation source" therefore should be taken to mean "radionuclide."

<i>Claim Language</i>	<i>Court's Construction</i>
"radiation source"	radionuclide

"Minimum prescribed dose"

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
Minimum prescribed dose received within a target tissue for delivering therapeutic effects.	Minimum dose needed to treat cancer cells.

The parties have requested construction of the phrase "minimum prescribed dose" and point out that the term appears in claims 2, 18, 24, 32, and 36 of the '204 patent. The parties do not argue that the term should be construed differently for different claims. However, claims 2, 24, 32, and 36 contain the phrase "minimum prescribed absorbed dose," and claim 18 contains the phrase "prescribed absorbed dose." These inconsistencies seem irrelevant, however, because the parties'

¹³ Cytyc also stated that this was an "Oxford comma" issue. Tr. at 137-38. However, in the sentence at issue, the Oxford comma is the one after "gamma radiation." Whether it is present does not alter the meaning of the sentence. Cytyc also argued that "we're in the land of eats, shoots and leaves." If Cytyc was referring to a book of such title, the court does not see how that would support Cytyc's argument; the theme of *Eats, Shoots & Leaves* is that punctuation should be used correctly. See Lynne Truss, *Eats, Shoots & Leaves: The Zero Tolerance Approach to Punctuation* (2004).

dispute is whether any such doses should be limited to treatment of cancer cells or allowed to cover any potential therapeutic effects. The court's construction of "brachytherapy" limits the claims to treatments "at or near a tumor or other proliferative tissue disease site." Xoft's proposed construction is too narrow, and Cytac's is too broad. However, in light of the construction of "brachytherapy," no construction of "minimum prescribed dose" or similar phrases is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"minimum prescribed dose"	(no construction necessary)

"Delivering a prescribed absorbed dose"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

Xoft argues that the patent does not reveal how one goes about prescribing a dose using the device, and that the phrase "delivering a prescribed absorbed dose" is therefore fatally indefinite. The '204 patent, however, describes a tool for treating proliferative tissue disease. A patent could adequately describe and claim a new apparatus or method for making the corrective curves in contact lenses, but a description of the particular curves a patient might require would not be necessary. If those skilled in the art would know how to use the disclosed invention, describing how to use it is unnecessary—the patentee merely needs to adequately describe the invention. Since Xoft bears the burden of proving that those skilled in the art would not know how to use the tool or method described in the patent and has presented no evidence on the subject, the court rejects Xoft's contention that the phrase is indefinite. No construction is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"delivering a prescribed absorbed dose"	(no construction necessary)

"The inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
The inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering	(indefinite)

"The inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"

<i>Cytec's proposed construction</i>	<i>Xoft's proposed construction</i>
Configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue.	(indefinite)

The phrases "the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose" and "configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose" are not indefinite for essentially the same reasons given in the previous section. As Cytec again appears to be attempting to impermissibly broaden its claims to capture any therapeutic effect, despite the clear limitation provided by the patentee's definition of "brachytherapy," the court also cannot adopt Cytec's proposed construction. No construction of the disputed language is necessary in light of the court's construction of other terms in the patent.

<i>Claim Language</i>	<i>Court's Construction</i>
"the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"	(no construction necessary)
"the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"	(no construction necessary)

"A minimum distance outward from the outer spatial volume expandable surface"

<i>Cytec's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

Claims 2, 24, 32, and 36 all include the phrase "the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface."¹⁴ Xoft asserts that "minimum distance" is indefinite in this context because the patent does not explain how the minimum distance is determined.

¹⁴ The court believes that one skilled in the art would understand that the patentee intended to define "target tissue" as the tissue "between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface." Taken literally, the patent explains the physical location where the act of defining "target tissue" takes place.

Here, "minimum" does not appear to add anything to the patent. The "target tissue" is the tissue outside of the outer chamber for a fixed distance in all directions, but this fixed distance or how one determines it are not explained. It seems that one skilled in the art would know how to determine the distance. *See* Tr. at 85-89. But the patent may as well read "a short distance outward" or "a determined distance outward" or merely "a distance outward."

Cytoc claims that specification provides some guidance and that the minimum distance may in some instances be between half and one centimeter. The specification does state that

device A can readily be configured to provide a dose in a therapeutic range, say between 40 to 60 Gray, at a distance between 0.5 and 1.0 cm from the outer spatial volume for an outer spatial volume having a diameter of 4.0 cm and being in contact with the resection cavity wall.

'204 patent, col. 6, ll. 31-35. However, Cytoc neglects to mention that "device A" is "an interstitial brachytherapy apparatus . . . such as those employed in U.S. Pat. No. 5,429,582, having a single spatial volume 50 filled with a radioactive material in solution." '204 patent, col. 6, ll. 3-7. In any case, this discussion does not use the phrases "target tissue" or "a minimum distance outward." Nevertheless, Xoft has presented no evidence that one skilled in the art would not understand the phrase "the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface." Xoft has not met its burden of proving by clear and convincing evidence that this language is indefinite, and the court finds that no construction is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"a minimum distance outward from the outer spatial volume expandable surface"	(no construction necessary)

"Controlled dose"

<i>Cytoc's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

"To reduce or prevent necrosis in healthy tissue proximate to the expandable surface"

<i>Cytoc's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

"Providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
Controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target issue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface	(indefinite)

Xoft argues that the patent does not reveal how one goes about controlling a dose using the device and that "reducing necrosis" is a hopelessly vague concept, making the '204 patent indefinite. Xoft, however, has presented no evidence that one skilled in the art would not be able to understand the patent and has again failed to meet its burden of proof. The court will therefore adopt Cytac's construction proposals. "Providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue" means "controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target issue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface."

<i>Claim Language</i>	<i>Court's Construction</i>
"controlled dose"	(no separate construction necessary)
"to reduce or prevent necrosis in healthy tissue proximate to the expandable surface"	(no separate construction necessary)
"providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue"	controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target issue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface

"Adapting the expandable surface to contact tissue surrounding the resection cavity to conform the tissue"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

Xoft's contention that this phrase is indefinite springs from its argument that "expandable surface element" means "deflated balloon or cage." As the court has rejected Xoft's interpretation of "expandable surface element," no construction of "adapting the expandable surface to contact tissue surrounding the resection cavity to conform the tissue" is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"adapting the expandable surface to contact tissue surrounding the resection cavity to conform the tissue"	(no construction necessary)

"Desired shape of the expandable surface element"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

Xoft has again presented no evidence to back up an argument that the phrase is indefinite and therefore again fails to carry its burden of proof. No construction of "desired shape of the expandable surface element" is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"desired shape of the expandable surface element"	(no construction necessary)

"Predetermined spacing"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

"A predetermined spacing is provided between said inner spatial volume and the expandable surface element" / "A predetermined spacing between said inner spatial volume and the expandable surface element"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
The distance between the inner spatial volume and the expandable surface element is determined in advance	(indefinite)

Xoft's contention that these phrases are indefinite is based on its argument that "expandable surface element" means "deflated balloon or cage," and Xoft has again presented no evidence to back up arguments that the phrases are indefinite. No construction of "predetermined spacing" is necessary. The court will adopt Cytyc's proposals and define both of the long phrases ("a predetermined spacing is provided between said inner spatial volume and the expandable surface element" and "a predetermined spacing between said inner spatial volume and the expandable surface element") as "the distance between the inner spatial volume and the expandable surface element is determined in advance."

<i>Claim Language</i>	<i>Court's Construction</i>
"predetermined spacing"	(no construction necessary)
"a predetermined spacing is provided between said inner spatial volume and the expandable surface element" / "a predetermined spacing between said inner spatial volume and the expandable surface element"	the distance between the inner spatial volume and the expandable surface element is determined in advance

"Intraoperatively"

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required) or During the surgical operation to remove proliferative tissue.	After surgical removal of tumor but prior to closing the surgical site

At the claim construction hearing, the parties appeared to agree on the definition of "interoperatively." See Tr. at 140. The previous apparent disagreement revolved around whether the surgical site could be closed before insertion of the catheter apparatus. The court understands that the parties agree that the catheter must be inserted before the surgical site is closed. The '204 patent at column 7, lines 55-64, specifically refers to the catheter being inserted "[f]ollowing tumor resection, but prior to closing the surgical site."

<i>Claim Language</i>	<i>Court's Construction</i>
"intraoperatively"	following tumor resection, but prior to closing the surgical site

"Solid radiation source"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
A radiation source that has a fixed shape and volume, and is not deformable	Solid radionuclide

The parties' primary dispute here is whether "radiation source" encompasses more than radionuclides, which the court addressed above to limit "radiation source" to radionuclides. Cytac presents a dictionary definition of "solid," namely, "of definite shape and volume; not liquid or gaseous," from the AMERICAN HERITAGE COLLEGE DICTIONARY, 1295 (3d ed. 1997). The court will therefore define "solid radiation source" as "a radionuclide of definite shape and volume; not liquid or gaseous."

<i>Claim Language</i>	<i>Court's Construction</i>
"solid radiation source"	a radionuclide of definite shape and volume; not liquid or gaseous

"The prescribed absorbed dose is delivered to the target tissue in substantially three dimensions"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
The prescribed absorbed dose is delivered to the target tissue such that all points at a given outward distance from the tissue wall will receive the same dose.	(indefinite)

Xoft contends that "prescribed absorbed dose" and "in substantially three dimensions" render "the prescribed absorbed dose is delivered to the target tissue in substantially three dimensions" fatally indefinite. The court has already rejected Xoft's argument regarding "prescribed absorbed dose."

Xoft points to Cytac's expert's testimony that "there's no such thing as substantially three dimensions" because something is either three dimensional or not. Mulville Decl. (dkt. # 51), Ex. L (Verhey Decl.) at 153. Cytac points to Xoft's expert's testimony that he could envision a brachytherapy apparatus that delivered 99 percent of its radiation in a plane; Cytac claims such a flat radiation field would not be in substantially three dimensions. Though a closer question than some of Xoft's other indefiniteness contentions, the court nonetheless finds that Xoft has not shown by clear and convincing evidence that one skilled in the art would not understand "in substantially three

1 dimensions" in the manner put forth by Cytyc. The court therefore adopts Cytyc's proposed
 2 construction for "the prescribed absorbed dose is delivered to the target tissue in substantially three
 3 dimensions," namely, "the prescribed absorbed dose is delivered to the target tissue such that all
 4 points at a given outward distance from the tissue wall will receive the same dose."

<i>Claim Language</i>	<i>Court's Construction</i>
"the prescribed absorbed dose is delivered to the target tissue in substantially three dimensions"	the prescribed absorbed dose is delivered to the target tissue such that all points at a given outward distance from the tissue wall will receive the same dose

United States District Court
For the Northern District of California

CLAIM CONSTRUCTION ORDER—No. C-05-05312 RMW
JAH

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III. ORDER

1. For the reasons given above, the court adopts the following claim construction as detailed in this order.

Term or phrase	Court's construction
"inner spatial volume"	a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere.
"outer, closed, inflatable chamber"	outer, closed, inflatable chamber
"predetermined constant spacing"	(no construction necessary)
"predetermined constant spacing between said inner spatial volume and radiation transparent wall"	spacing predetermined by one skilled in the art between the wall or edge of the inner spatial volume and the radiation transparent wall of the outer, closed, inflatable chamber, when inflated, which is constant in all directions if the outer chamber is spherical, or constant along a radial plane if the outer chamber is not spherical
"rendering uniform"	to make the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument
"Means . . . for rendering uniform the radial absorbed dose profile of the emissions"	Function: Making the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument. Structure: A radiation absorbing or attenuating material, <i>e.g.</i> , air, x-ray contrast fluid, contrast media used in angiography, water, a gas, or barium sulfate or their equivalents.
"The radioactive material"	The material of claim 1 containing a radionuclide.
"A plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile"	(no construction needed)
"interstitial"	involving a surgically-created cavity in a body
"brachytherapy"	radiation therapy delivered by a spatially-confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site
"interstitial brachytherapy"	(no construction necessary)

CLAIM CONSTRUCTION ORDER—No. C-05-05312 RMW
JAH

"outer spatial volume"	a region of space defined by an expandable surface element and surrounding an inner "expandable surface element"(no construction needed)
"radiation source"	radionuclide
"minimum prescribed dose"	(no construction necessary)
"delivering a prescribed absorbed dose"	(no construction necessary)
"the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"	(no construction necessary)
"the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"	(no construction necessary)
"a minimum distance outward from the outer spatial volume expandable surface"	(no construction necessary)
"controlled dose"	(no separate construction necessary)
"to reduce or prevent necrosis in healthy tissue proximate to the expandable surface"	(no separate construction necessary)
"providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue"	controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target issue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface
"adapting the expandable surface to contact tissue surrounding the resection cavity to conform the tissue"	(no construction necessary)
"desired shape of the expandable surface element"	(no construction necessary)
"predetermined spacing"	(no construction necessary)
"a predetermined spacing is provided between said inner spatial volume and the expandable surface element" / "a predetermined spacing between said inner spatial volume and the expandable surface element"	the distance between the inner spatial volume and the expandable surface element is determined in advance
"intraoperatively"	following tumor resection, but prior to closing the surgical site
"solid radiation source"	a radionuclide of definite shape and volume; not liquid or gaseous

"the prescribed absorbed dose is delivered to the target tissue in substantially three dimensions"

the prescribed absorbed dose is delivered to the target tissue such that all points at a given outward distance from the tissue wall will receive the same dose

2. The parties shall appear for a further case management conference on June 1, 2007 at 10:30 a.m. and shall file a further joint case management conference statement no later than four days prior.

DATED: 4/27/07

Ronald M. Whyte
 RONALD M. WHYTE
 United States District Judge

United States District Court
 For the Northern District of California

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12 Dated: 4/27/07

13 SPT
14 Chambers of Judge Whyte

15 CLAIM CONSTRUCTION ORDER—No. C-05-05312 RMW
16 JAH

17 31

United States District Court
For the Northern District of California

Exhibit 5

#7/A



PATENT APPLICATION

OUR FILE NO. 970344.ORI

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re App : Jeffery A. Williams, et al.
S.N. : 08/900,021 : September 1, 1998
Filed : July 24, 1997 : Art Unit 3736
For : DOUBLE WALL BALLOON CATHETER
FOR TREATMENT OF
PROLIFERATIVE TISSUE : Examiner J. Lacyk

ASSISTANT COMMISSIONER FOR PATENTS

WASHINGTON, D.C. 20231

Dear Sir:

Responsive to the first Official Action of May 12, 1998,
please amend the above-captioned application as follows:

IN THE CLAIMS:

Please cancel Claim 12.

Please amend the following claims:

1 (Amended). Apparatus for delivering radioactive
emissions to a body location with a [controlled] uniform
radiation profile, comprising:

(a) a catheter body member having a proximal end and
distal end;

(b) an inner spatial volume disposed [at] proximate
the distal end of the catheter body member;

(c) an outer, closed, [distensible] inflatable
chamber defined by a radiation transparent wall [disposed at]

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affixed to the body member proximate the distal end [of the body member] thereof in surrounding relation to the inner spatial volume with a predetermined constant spacing between said inner spatial volume and the radiation transparent wall;

(d) a material containing a radionuclide(s) disposed in one of the inner spatial volume and outer chamber; and

(e) means disposed in the other of the inner spatial volume and outer chamber for [controlling] rendering uniform the radial absorbed dose profile of the emissions from the one of the inner spatial volume and outer chamber containing the radionuclides.

2 (Amended). The apparatus as in Claim 1 wherein said inner spatial volume is an inner closed, [distensible] chamber defined by a further radiation transparent wall.

3 (Amended). The apparatus of Claim 1 wherein the means for [controlling] rendering uniform the absorbed dose profile is a radiation attenuating material.

4 (Amended). The apparatus of Claim [2] 3 wherein the radiation [absorbing fluid] attenuating material is selected from a group consisting of barium sulphate, water, and X-ray contrast media.

8 (Amended). The apparatus as in Claim [1] 2 wherein the inner chamber contains the radioactive material.

10 (Amended). The apparatus as in [any one of Claims 7 or] Claim 8 wherein the radioactive material is a fluid.

11 (Amended). The apparatus as in [any one of Claims 7 or]

11 Claim 8 wherein the radioactive material is a solid.

12 12 (Amended). The apparatus as in Claim 1 wherein the material containing a radionuclide comprises a plurality of

15 radioactive solid particles [are] placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile.

1 Please add the following claim:

13 14. The apparatus as in Claim 2 wherein the inner and outer chambers are spherical in shape and are concentric.

R E M A R K S

This Amendment is submitted in response to the first Official Action of May 12, 1998. Reconsideration and allowance of Claims 1-11 and 13, as presently amended, are respectfully requested.

The present invention is directed to an apparatus for treating proliferative tissue disorders by delivering radioactive emissions to target tissue within the body with a uniform radial absorbed dose profile whereby diseased tissue may be irradiated with sufficient intensity to kill disease cells, but without producing necrosis of neighboring healthy tissue. With the apparatus of the present invention, it is possible to deliver a desired radiation dose at a predetermined radial distance from a source of radioactivity by providing a catheter body member having an inner spatial volume disposed proximate the distal end of the catheter body and with an outer, closed, inflatable,

chamber defined by a radiation transparent wall affixed to the body member proximate the distal end thereof in a surrounding relation to the inner spatial volume with a predetermined constant spacing between the inner spatial volume and the radiation transparent wall. A material containing a radionuclide is introduced through the catheter body in either the inner spatial volume or the outer chamber and the other of the inner spatial volume or outer chamber not containing the radionuclide is made to contain a radiation attenuating material for rendering uniform the radial absorbed dose profile of the emissions from the one of the inner spatial volume and outer chamber that contains the radionuclide.

In the Official Action, objection was raised to Claims 4 and 13 under 35 U.S.C. §112, second paragraph, as being indefinite. Claim 13 has been amended to clarify that the material containing a radionuclide as recited in claim 1 comprises "a plurality of radioactive solid particles". Claim 4 has been amended by changing "radiation absorbing fluid" to -- radiation attenuating material --, the latter phrase finding an antecedent in Claim 3 from which it now depends.

Concerning the rejection on the merits, Claims 1-5, 8 and 10 were rejected under 35 U.S.C. §102(b) as being anticipated by Ishiwara et al. This rejection is respectfully traverse. Before it is appropriate to find a claim anticipated under 35 U.S.C. §102(b), it is necessary to find within the four corners of the prior art reference relied upon a full teaching of each and every

A

element of the claims sought to be anticipated. As Claim 1 has now been amended, it calls for an outer, closed, inflatable chamber located proximate the distal end of a catheter body member in surrounding relation to an inner spatial volume such that there is a predetermined constant spacing between the inner spatial volume and the radiation transparent wall. There is then provided a means disposed in the chamber, not having the radiation source, a substance for rendering uniform the radial absorbed dose profile of the emissions from the chamber that contains the radiation source. In the Ishiwara et al. '360 patent relied upon for anticipation, the outer chamber defined by the radiation transparent wall 12 cannot provide a uniform radiation profile. The outer balloon 12 in the Ishiwara et al. patent functions only to stabilize the device within and hold a thermal mass (liquid) against surrounding tissue so that it can be warmed or cooled by thermal conduction. There is no teaching or suggestion in the patent of how to provide a uniform radial absorbed dose profile of emissions emanating from the liquid radiation source 38. Moreover, given the banana shape of the Ishiwara device, the profile will be much different proximate the distal and proximal ends of the balloon 12 than in its central tissue contacting region. Thus, it cannot be said that applicants' invention, as claimed, is taught by or inherent in the Ishiwara '360 device.

Given the above mentioned differences, neither Claim 1 nor any of the remaining dependent claims is anticipated by the

Ishiwara et al. teachings. It is further submitted that the invention of Claim 1 is not rendered obvious from the teachings of the Ishiwara et al. patent.

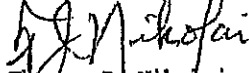
While admittedly the present invention and the device described in the Ishiwara et al. patent have some points of similarity, i.e., both are catheters having an outer closed inflatable chamber and an inner spatial volume surrounded by the outer chamber and both are designed to provide radiation therapy to a tumor site, that is where the similarity ends. Applicants' invention is specifically designed to provide a uniform radial absorbed dose profile of the emissions from the particular chamber containing the radionuclide material so that occurrences of "hot spots" and/or "cold spots" are substantially eliminated. Hot spots can result in necrosis of healthy tissue, a condition to be avoided, while cold spots may mean that cancerous cells are not irradiated and killed. In one embodiment, uniformity of the radial absorbed profile is achieved by providing a spherical outer chamber which when inflated to contact the margins resulting following surgical removal of the tumor, a desired constant spacing will be maintained between the radiation source and the adjacent tissue structures. In a second embodiment, attention is paid to the spacing between the inner and outer radiation transparent walls so that it is constant over the entire surfaces of the two chambers. Given these important distinctions which are neither taught nor suggested by the Ishiwara reference, applicants' independent Claim 1, as amended,

is not made obvious from the prior art. In fact, it is proper to say that the Ishiwara et al. reference teaches away from applicants' invention given the elongate, cylindrical shape of the radiation source employed and the oblong-shaped outer balloon surrounding it.

In that Claim 1, as amended, has been shown to be patentable over the prior art, and because Claims 2-11 and 13 depend directly or indirectly from Claim 1, all of the claims remaining in the application are believed to be in condition for allowance and a Notice to that effect is respectfully solicited.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that the foregoing Amendment in response to the Official Action of May 12, 1998 in application Serial No. 08/900,021 of inventors, Jeffery A. Williams et al., filed July 24, 1997, for "DOUBLE WALL BALLOON CATHETER FOR TREATMENT OF PROLIFERATIVE TISSUE" is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on September 1, 1998.

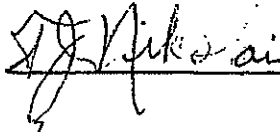


Exhibit 6

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7

8

UNITED STATES DISTRICT COURT

9

NORTHERN DISTRICT OF CALIFORNIA

10

SAN JOSE DIVISION

11 XOFT, INC.,

12 Plaintiff,

13 vs.

14 CYTYC CORPORATION and PROXIMA
THERAPEUTICS, INC.,

15 Defendants.

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17

AND RELATED COUNTERCLAIMS.

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) Case No. CV 05-05312 RMW

)
) **DEFENDANT AND COUNTERCLAIMANT**
) **CYTYC CORPORATION'S OPENING**
) **CLAIM CONSTRUCTION BRIEF (PAT.**
) **L.R. 4-5(a))**

) Tutorial and Markman Hearing
) Date: December 20, 2006
) Time: To Be Set
) Room: Courtroom 6, 4th Floor
) Judge: Hon. Ronald M. Whyte

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STATUTES

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1 Pursuant to the Agreed Scheduling Order,¹ Defendant and Counterclaimant Cytyc Corporation
2 ("Cytyc") respectfully submits this Brief addressing the construction of disputed terms, phrases and
3 clauses in the asserted claims of U.S. Patent Nos. 5,913,813 (the "'813 patent") and 6,413,204 (the
4 "'204 patent") (attached hereto as Exhibits A and B to the Declaration of Henry C. Su, respectively).
5 Cytyc currently asserts claims 1, 2, 3, 4, 8 and 12 of the '813 patent and claims 1, 2, 3, 4, 8, 16, 17, 18,
6 19, 20, 21, 23, 24, 25, 26, 30, 32, 34, 35 and 36 of the '204 patent against Plaintiff Xoft, Inc. ("Xoft").

7 PRELIMINARY STATEMENT

8 The differences in the parties' approaches to construing the disputed terms are stark. Cytyc's
9 proposed constructions are straightforward, applying the plain meaning that would be apparent to one
10 of ordinary skill in the art when the disputed terms are read in light of the specification, in accordance
11 with the Federal Circuit's recent *en banc* decision in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir.
12 2005) (*en banc*), *cert. denied*, 126 S. Ct. 1332 (2006). In contrast, Xoft insists on improperly injecting
13 into its proposed constructions of the disputed terms limitations that are nowhere found in the claim
14 language and are not supported by the specification, in contravention of Federal Circuit law. Xoft also
15 repeatedly attempts to limit the claim terms to exemplary embodiments in the specification, which is
16 also contrary to the law. In a few instances where the patent specifically defines a claim term, Xoft
17 refuses to acknowledge that express definition, crafting instead its own definition from whole cloth.
18 Finally, Xoft cannot hope to establish by clear and convincing evidence that certain claims terms are
19 indefinite. The testimony of Cytyc's expert, Dr. Lynn J. Verhey, shows that one skilled in the art,
20 reading the disputed terms in light of the specification, understands exactly what is being claimed.
21 Xoft's strained interpretations of the disputed terms and its meritless allegations of indefiniteness
22 should thus be rejected.

23
24
25 ¹ The Agreed Scheduling Order called for Cytyc to file its Opening Claim Construction Brief on November 6, 2006. On
26 account of the fact that the Court was moving the date for the technology tutorial and claim construction hearing from
27 December 6-7, 2006 to December 20, 2006, the parties filed on November 3, 2006 a joint stipulation and proposed order
28 requesting that the Court enlarge the briefing schedule. On November 7, 2006, the Court declined to enlarge the briefing
schedule (other than to set the due date for the reply brief on December 7, 2006) and held that "[h]aving at least the
minimum time periods set forth in Civil L.R. 7 to consider the parties' arguments would be particularly useful to the court
in a case such as this." In response to this order, Cytyc moved promptly to finalize and file its Opening Claim Construction
Brief, which is still being submitted more than 35 days before the scheduled hearing date.

BACKGROUND

I. THE TECHNOLOGY

The patents-in-suit relate to the field of treating proliferative tissue diseases like cancer with radiation. Traditionally, a patient diagnosed with a cancerous tumor would have the tumor removed and then the region of body where the tumor was located would be exposed to an external radiation beam in an attempt to ensure that any remaining cancerous cells are destroyed. One of the major disadvantages of external beam radiation therapy is that it is difficult to target just the diseased area and avoid irradiating significant portions of healthy tissue. Accordingly, it is medically desirable to use various devices and instruments to position the radiation source as close as possible to the diseased site. This technique is known as brachytherapy. The root "brachy" comes from the Greek word for "short distance."

The patents-in-suit are directed specifically to a type of brachytherapy known as interstitial brachytherapy, in which the radiation source is introduced in close proximity to diseased cells that are within the interstices of a body tissue. This technique requires creating some sort of path through the tissue to reach the targeted site, and it can be contrasted with brachytherapy in which the radiation source is merely inserted into a natural body cavity like the bladder (intracavitary), into a body lumen like the urethra (intraluminal), or on the surface of the body (surface brachytherapy). For example, as taught by the patents-in-suit, a radiation source is introduced through the opening and cavity created by the tumor resection so that it can treat the diseased cells within the interstices of the tissue at the margins of the tumor resection site.

According to the invention described and claimed in the patents-in-suit, the radiation source is introduced into the resection cavity using a catheter. An expandable or inflatable device, such as a cage or balloon, is used to shape the resection cavity so that the radiation dose absorbed by the diseased cells within the interstices of the tissue at the margins of the cavity is made more uniform. Three primary factors affect the amount of the absorbed dose: (1) distance of the tissue to be treated from the radiation source, (2) the presence of a radiation attenuating medium such as air or a saline solution, and (3) the use of radiation shielding.

1 The patents-in-suit use these factors, individually or in combination, to improve treatment by
2 controlling the "radial absorbed dose profile" and the "three-dimensional isodose profile." The former
3 involves controlling the absorbed dose as a function of radial distance from the radiation source to
4 points within the targeted tissue; the latter involves conforming the shape of the targeted tissue to a
5 virtual, three-dimensional surface defined by points receiving the same radiation dose. To control the
6 radial absorbed dose profile, one may surround the radiation source with a radiation attenuating
7 medium to minimize the ratio of the absorbed dose at the wall of the tumor cavity to the dose within
8 the interstices of the target tissue. If the ratio is too high, then "hot spots" can occur at the wall of the
9 cavity, which cause healthy tissue to necrose. Controlling the three-dimensional isodose profile
10 involves shaping the resected tumor cavity and adjusting the position of the radiation source relative to
11 the cavity to create a desired, virtual isodose surface on which all points receive substantially the same
12 dose. These points will be coincident with points within the interstices of the tissue to be treated.

13 II. THE EXPERTS

14 Although Cytac bases its proposed constructions on the intrinsic evidence, *i.e.*, the patents'
15 claim language, specifications, and prosecution histories, Cytac also proffers the testimony of Dr.
16 Lynn J. Verhey to provide the perspective of one skilled in the relevant art. *Phillips*, 415 F.3d at 1313
17 (claims must be construed from the perspective of one skilled in the art). In this case, a person of
18 ordinary skill in the art has a background in radiation oncology physics with a focus on brachytherapy.
19 Such individuals would hold a M.S. degree in Physics or Engineering, with 3 or more years of clinical
20 medical physics experience, or a Ph.D. in Physics or Engineering with 2 or more years of clinical
21 experience. (See Exhibit D to the Declaration of Henry C. Su (Declaration of Lynn J. Verhey, Ph.D.
22 ("Verhey Rep.)) at 4:6-18.)

23 Dr. Verhey is an expert in the field of radiation oncology, with decades of experience. He is
24 currently a Full Professor and Vice-Chair in the Department of Radiation Oncology at University of
25 California, San Francisco. Dr. Verhey earned a Ph.D. in Physics and, in 1975, took a position as
26 Hospital Radiation Physicist at Massachusetts General Hospital (MGH) with a concurrent continuing
27 position as Assistant Professor at the Harvard Medical School. In 1990, he became Chief of the
28 Physics Division and Associate Professor in the Department of Radiation Oncology at UCSF. He has

1 taught courses in physics, radiation, and medical physics (including radiation oncology). He has
2 conducted research on new methods of delivering radiation to cancer patients and has published over
3 100 technical papers in that field. Dr. Verhey is a certified Therapeutic Radiological Physicist by the
4 American Board of Radiology and is a fellow in the American Association of Physics in Medicine and
5 the American Society of Therapeutic Radiology and Oncology. In sum, he is a well-recognized and
6 independent expert in methods of delivering radiation to cancer patients.

7 By contrast, Xoft's expert, Paul A. Lovoi, Ph.D., did not attach a curriculum vitae to his report
8 and his credentials in the relevant field are not otherwise apparent. Moreover, Dr. Lovoi is not
9 independent. He is one of the founders of Xoft and was an officer of Xoft until recently. He now
10 consults for Xoft and has worked for the company during the last decade. His report indicates a Ph.D.
11 in physics but does not list any specific experience in the field of radiation oncology, other than 9 years
12 of purported experience in "medical use of sources of radiation." Xoft is Dr. Lovoi's company – he
13 founded it, he ran it, and he has devoted a good part of his life to it. This Court should weigh his
14 opinions accordingly.

15 APPLICABLE LAW

16 Sitting *en banc*, the Federal Circuit recently clarified its guiding principles for construction of
17 patent claims. *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005). In *Phillips*, the court
18 emphasized the "primary importance" of the language of the claims themselves:

19 It is a "bedrock principle" of patent law that "the claims of a patent define the invention
20 to which the patentee is entitled the right to exclude." . . . That principle has been
21 recognized since at least 1836, when Congress first required that the specification
22 include a portion in which the inventor "shall particularly specify and point out the part,
23 improvement, or combination, which he claims as his own invention or discovery." . . .
24 In the following years, the Supreme Court made clear that the claims are "of primary
importance, in the effort to ascertain precisely what it is that is patented." . . . Because
the patentee is required to "define precisely what his invention is," the Court explained,
it is "unjust to the public, as well as an evasion of the law, to construe it in a manner
different from the plain import of its terms." . . .

25 415 F.3d at 1312 (citations omitted). The Federal Circuit also reaffirmed the time-honored rule that
26 claim terms are generally to be given their ordinary and customary meaning to those skilled in the art:

27 We have frequently stated that the words of a claim "are generally given their ordinary
28 and customary meaning." . . . We have made clear, moreover, that the ordinary and
customary meaning of a claim term is the meaning that the term would have to a person
of ordinary skill in the art in question at the time of the invention, i.e., as of the effective

1 filing date of the patent application. . . . The inquiry into how a person of ordinary skill
2 in the art understands a claim term provides an objective baseline from which to begin
claim interpretation.

3 *Id.* at 1312-13 (citations omitted). Likewise, the court stressed that claims must be read in light of the
4 specification. *Id.* at 1315 (“claims must be read in view of the specification, of which they are a part.”)
5 (internal quotations omitted)). Importantly, the court held that claim terms should be given “*their*
6 *broadest reasonable construction* ‘in light of the specification as it would be interpreted by one of
7 ordinary skill in the art.’” *Id.* at 1316 (citing *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364
8 (Fed. Cir. 2004) (emphasis added)).

9 The *Phillips* court repeated the venerable warning that one must “avoid the danger of reading
10 limitations from the specification into the claim.” 415 F.3d at 1323. With that warning in mind, the
11 court described the two primary instances in which the specification can limit the meaning of claim
12 terms. *First*, the patentee can choose to recite an explicit definition for a claim term in the
13 specification. *Id.* at 1316. In that case it is said that the patentee has acted as his own lexicographer
14 and the patentee’s definition “governs.” *Id.* *Second*, the specification may limit the plain meaning of a
15 claim term when the patentee disclaims or disavows certain interpretations of the term. *Id.* In other
16 words, the specification can limit the plain meaning of claim terms when the patentee has clearly set
17 forth a limiting interpretation.

18 The prosecution history is also important to consider when construing claim terms. The
19 *Phillips* court explained:

20 [W]e have held that a court “should also consider the patent’s prosecution history, if it
21 is in evidence.” . . . The prosecution history, which we have designated as part of the
22 “intrinsic evidence,” consists of the complete record of the proceedings before the PTO
23 and includes the prior art cited during the examination of the patent. . . . Like the
specification, the prosecution history provides evidence of how the PTO and the
inventor understood the patent. . . . Furthermore, like the specification, the prosecution
history was created by the patentee in attempting to explain and obtain the patent.

24 415 F.3d at 1317 (citations omitted).

25 The *Phillips* court also noted that expert testimony (on which Xoft almost exclusively relies in
26 this case) should play a lesser role in claim construction. 415 F.3d at 1317 (“[W]hile extrinsic
27 evidence ‘can shed useful light on the relevant art,’ we have explained that it is ‘less significant than
28

1 the intrinsic record in determining the legally operative meaning of claim language.”) (internal
2 quotations omitted). The court added that:

3 extrinsic evidence in the form of expert testimony can be useful to a court for a variety
4 of purposes, such as to provide background on the technology at issue, to explain how
5 an invention works, to ensure that the court’s understanding of the technical aspects of
6 the patent is consistent with that of a person of skill in the art, or to establish that a
7 particular term in the patent or the prior art has a particular meaning in the pertinent
8 field. . . . However, conclusory, unsupported assertions by experts as to the definition
9 of a claim term are not useful to a court. Similarly, *a court should discount any expert
10 testimony “that is clearly at odds with the claim construction mandated by the claims
11 themselves, the written description, and the prosecution history, in other words, with the
12 written record of the patent.”*

13 *Id.* at 1318 (emphasis added; citations omitted).

14 One claim limitation from the ‘813 patent uses the term “means,” which creates a presumption
15 that the limitation is drafted in “means plus function” format pursuant to 35 U.S.C. § 112, ¶ 6.
16 *Greenberg v. Ethicon Endo-Surgery, Inc.*, 91 F.3d 1580, 1584 (Fed. Cir. 1996). “Construction of a
17 means plus function limitation requires identification of the function recited in the claim and a
18 determination of what structures have been disclosed in the specification that correspond to the means
19 for performing that function.” *Epcon Gas Sys., Inc. v. Bauer Compressors, Inc.*, 279 F.3d 1022, 1032
20 (Fed. Cir. 2002). Structure described in the specification constitutes “corresponding structure” if the
21 specification “clearly links or associates that structure to the function recited in the claim.” *Kahn v.*
22 *General Motors Corp.*, 135 F.3d 1472, 1476 (Fed. Cir. 1998).

23 The Federal Circuit has held that a claim must be “definite” enough to be understood by one
24 skilled in the art:

25 We have stated the standard for assessing whether a patent claim is sufficiently definite
26 to satisfy the statutory requirement as follows: If one skilled in the art would understand
27 the bounds of the claim when read in light of the specification, then the claim satisfies
28 section 112 paragraph 2.

29 *Exxon Research & Eng’g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001) (citing *Miles*
30 *Labs., Inc. v. Shandon, Inc.*, 997 F.2d 870, 875 (Fed. Cir. 1993)). “If the meaning of the claim is
31 discernible, even though the task may be formidable and the conclusion may be one over which
32 reasonable persons will disagree, we have held the claim sufficiently clear to avoid invalidity on
33 indefiniteness grounds.” *Id.* See also *Fresenius Med. Care Holdings, Inc. v. Baxter Int’l, Inc.*, No. C

1 03-1431 SBA, 2006 U.S. Dist. LEXIS 36788, at *51 (N.D. Cal. May 24, 2006). As the party asserting
2 invalidity, Xoft bears the burden of proving indefiniteness. Moreover, because patents enjoy a
3 statutory presumption of validity, Xoft's burden is heightened – it must prove its case with clear and
4 convincing evidence. *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1375
5 (Fed. Cir. 1986). A claim is not indefinite merely because it poses a difficult issue of claim
6 construction (which is not even the case here, where construction is straightforward); if the claim can
7 be construed at all, then it is not invalid for indefiniteness. *See, e.g., Bancorp Servs., LLC v. Hartford*
8 *Life Ins. Co.*, 359 F.3d 1367, 1371 (Fed. Cir. 2004). Thus, the biased, conclusory statements of Xoft's
9 expert alone cannot establish indefiniteness by clear and convincing evidence. *See Intel Corp. v. VIA*
10 *Techs.*, 319 F.3d 1357, 1367 (Fed. Cir. 2003) (expert's conclusory statements are insufficient to
11 provide clear and convincing evidence of indefiniteness).

12 CONSTRUCTION OF CLAIM TERMS²

13 I. TERMS IN THE '813 PATENT

14 The claims of the '813 patent relate to an instrument comprising a concentric arrangement of an
15 inner spatial volume and an outer spatial volume defined by an inflatable chamber, disposed near the
16 distal end of a catheter body. One of the volumes contains a source of radiation, while the other
17 volume may contain a radiation absorptive material. In one preferred embodiment, shown in Figure 1
18 of the patent, the inner volume is defined by an enclosed chamber surrounding the catheter body and
19 containing a radioactive source. The outer chamber, concentric with the inner volume, is then inflated
20 with air or other radiation absorbing material so that its wall contacts the wall of the surgical cavity
21 substantially at all points. The distance between the radiation source and the wall of the outer chamber
22 can be made constant. This embodiment permits the controlled delivery of radiation to a layer of tissue
23 surrounding the surgical cavity.³ By manipulating the volume and type of material in the outer
24

25 _____
26 ² Cytyc addresses herein only those terms about which the parties disagree and which Cytyc believes to be material to
27 resolution of this suit. As to terms not addressed, Cytyc's position is as set forth in the parties' Joint Claim Construction
28 Statement, which Cytyc incorporates by reference herein.

³ The tissue to be treated and the resected cavity can be thought of as an orange peel with the fruit (*i.e.*, the tumor)
removed. A radiation source is placed within the space previously occupied by the fruit. The thickness of the "orange

(Continued...)

1 chamber, the ratio of the absorbed dose at the surface of the wall of tissue to the dose at the tissue
2 depth where the minimum dose is prescribed to be received can be controlled so as to maximize the
3 effectiveness of the treatment and minimize adverse side effects, namely, unwanted necrosis of healthy
4 tissue.

5 The '813 patent teaches that other embodiments can be used to deliver therapeutic radiation to
6 the layer of tissue surrounding the surgical cavity. (Col 2:64 – 4:20; FIGS. 3-5.) These other
7 embodiments include the use of a radioactive liquid within an inner inflatable chamber, a plurality of
8 radioactive solid particles, a slurry of a fluid containing particles of a radioactive isotope or a solid
9 radioactive source. Alternatively, these same radiation sources can be placed in the volume of space
10 between the inner chamber and the outer inflatable chamber. Any of these embodiments might be used
11 as a means of delivering radiation to tissue within the wall of a surgical cavity.

12 **A. “Inner Spatial Volume” (All Asserted Claims)**

Cytac's Proposed Construction	Xoft's Proposed Construction
A region of space surrounded by an outer spatial volume that is defined by a closed inflatable chamber.	Inner balloon in two-balloon device or spherical solid radionuclide in one-balloon device.

17 Xoft's attempt to limit the “inner spatial volume” to a “balloon” or a “spherical solid
18 radionuclide” should be rejected. As an initial matter, a “balloon” is not even one of the embodiments
19 of the “inner spatial volume” described in the specification. Rather, the specification describes, as an
20 exemplary embodiment, that “the inner spatial volume 30 . . . may be defined by a generally spherical
21 polymeric film wall 32.” (Col. 2:35-36 (emphasis added).) In any event, it is improper to limit the
22 claim language to the embodiments in the specification, as Xoft proposes. *Phillips*, 415 F.3d at 1323
23 (“For instance, although the specification often describes very specific embodiments of the invention,
24 we have repeatedly warned against confining the claims to those embodiments.”).

25
26 (...Continued)

27 peel” corresponds to the thickness of the tissue to be treated – in most procedures the “orange peel” of tissue to be treated is
28 about 2 centimeters thick. (See, e.g., '813 patent at FIG. 4.)

1 More fundamentally, Xoft confuses the tangible structure that defines the inner spatial volume
2 with the volume itself. The specification provides that the inner spatial volume 30 “may be defined by
3 a generally spherical polymeric film.” The film defines the boundary of the volume but the volume is
4 the region of space within that boundary. (Exhibit C to the Declaration of Henry C. Su (American
5 Heritage College Dictionary (“AHC”)) at 1513.) Thus, according to the specification, the inner spatial
6 volume is simply a region of space surrounded by an outer spatial volume. (See col. 1:52-55 (“a first
7 spatial volume at the distal end of a catheter and a second spatial volume defined by a surrounding of
8 the first spatial volume by a polymeric film wall”)).

9 Cytac’s proposed construction fully captures the plain meaning of “inner spatial volume,”
10 which the Federal Circuit notes is of “primary importance” in claim construction. *Phillips*, 415 F.3d at
11 1312. A “spatial volume” is a commonly understood English term, meaning simply “a region of
12 space.” (AHC at 1513.) The word “inner” means that that region of space is located within something
13 else, and the specification provides that that “something else” is another (outer) “spatial volume.”
14 (Col. 1:52-55.) “Inner spatial volume” should therefore be construed to mean “a region of space
15 surrounded by an outer spatial volume that is defined by a closed inflatable chamber.”

16 **B. “Outer, Closed, Inflatable Chamber” (All Asserted Claims)**

Cytac’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Inflatable balloon, i.e., deflated balloon.

20 Cytac believes that no construction of this term is required or appropriate. The term has its
21 ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic
22 evidence. There is no evidence of any intent by the inventors to impart a novel or special meaning to
23 the term and Xoft has pointed to none. As discussed above with respect to an “inner spatial volume,”
24 Xoft’s construction improperly attempts to limit the claim term to just a balloon. But nothing in the
25 specification limits the outer, closed inflatable chamber to a “balloon.” Xoft’s proposed construction is
26 not supported by the specification and is contrary to law. Cytac proposes the term be given its plain
27 meaning: an “outer, closed, inflatable chamber.” Examples of such a chamber include an inflatable
28 balloon or an expandable cage, and as Dr. Verhey points out, an “inflatable chamber of any type”

1 could satisfy this limitation. This, Xoft's proposed construction should be rejected and the plain
2 meaning of the term adopted.

3 **C. "Predetermined Constant Spacing" (All Asserted Claims)**

Cytyc's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Indefinite. "Predetermined" spacing is some undefined constant spacing predetermined in some undefined manner with regard to deflated outer chamber.

9 Cytyc addresses the construction of this term in connection with its construction of the term "a
10 predetermined constant spacing between said inner spatial volume and the radiation transparent wall"
11 below. Cytyc believes that a separate construction of this term divorced from the context of the
12 surrounding claim language is neither required nor appropriate. *See Phillips*, 415 F.2d at 1314 ("Quite
13 apart from the written description and the prosecution history, the claims themselves provide
14 substantial guidance as to the meaning of particular claim terms. . . . To begin with, the context in
15 which a term is used in the asserted claim can be highly instructive.") (citing *ACTV, Inc. v. Walt*
16 *Disney Co.*, 346 F.3d 1082, 1088 (Fed. Cir. 2003) ("the context of the surrounding words of the claim
17 also must be considered in determining the ordinary and customary meaning of those terms")).

18 Xoft proposes no construction of this term, arguing that it is indefinite. Contrary to Xoft's
19 assertion, the term "predetermined constant spacing" is not indefinite and has an ordinary and
20 customary meaning to one skilled in the art. Dr. Verhey easily understood the phrase "predetermined
21 constant spacing" – indeed, any speaker of English can understand it – to mean that the spacing
22 between the inner spatial volume and the wall of the outer inflatable chamber is made to be
23 substantially constant. This spacing is "predetermined" in the sense that it is chosen in advance by one
24 skilled in the art. (Exhibit C at 1077.) Although Xoft incorrectly suggests that the patent must
25 describe that amount of spacing, a patent does not need to describe what one skilled in the art already
26 knows. *See S3 Inc. v. nVidia Corp.*, 259 F.3d 1364, 1371 (Fed. Cir. 2001) ("The law is clear that
27 patent documents need not include subject matter that is known in the field of the invention and is in
28 the prior art, for patents are written for persons experienced in the field of the invention. . . . To hold

otherwise would require every patent document to include a technical treatise for the unskilled reader.”) (citation omitted). One skilled in the art knows how to determine an appropriate “predetermined constant spacing.” Xoft cannot possibly show that the term is indefinite by clear and convincing evidence.

D. “Predetermined Constant Spacing Between Said Inner Spatial Volume And The Radiation Transparent Wall” (All Asserted Claims)

Cytec’s Proposed Construction	Xoft’s Proposed Construction
The spacing between the inner spatial volume and the radiation transparent wall of the outer, closed, inflatable chamber, when inflated, can be made constant in all directions if the outer chamber is spherical, or constant along a radial plane if the outer chamber is not spherical.	Indefinite. See “predetermined constant spacing,” <i>supra</i> , § I.C.

Xoft proposes no construction of this term, arguing only that it is indefinite. The conclusory statement of Dr. Lovoi, who works for Xoft and thus cannot provide a neutral opinion, does not come close to providing the clear and convincing evidence needed for Xoft to show indefiniteness. To the contrary, the term is readily understood by those skilled in the art. As Dr. Verhey explains, the term means that the spacing between the inner spatial volume and the radiation transparent wall of the outer, closed inflatable chamber, when inflated, can be made constant. If the outer chamber is spherical, then the distance is constant in all directions. If the outer chamber is cylindrical, then the distance is constant around a radial plane that is perpendicular to the axis of the catheter. (Verhey Rep. at 7:2-5.) This plain meaning construction should be adopted. *Phillips*, 415 F.3d at 1312 (plain meaning is of “primary importance”).

E. “Rendering Uniform” (All Asserted Claims)

Cytec’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Making the same, i.e., causing to have the same value or characteristic at all points.

Cytec addresses the construction of this term in connection with its construction of the term “means . . . for rendering uniform the radial absorbed dose profile of the emissions” below. Cytec

believes that a separate construction of this term divorced from the context of the surrounding claim language is neither required nor appropriate. *See Phillips*, 415 F.3d at 1314.

F. “Means . . . For Rendering Uniform The Radial Absorbed Dose Profile Of The Emissions “ (All Asserted Claims)

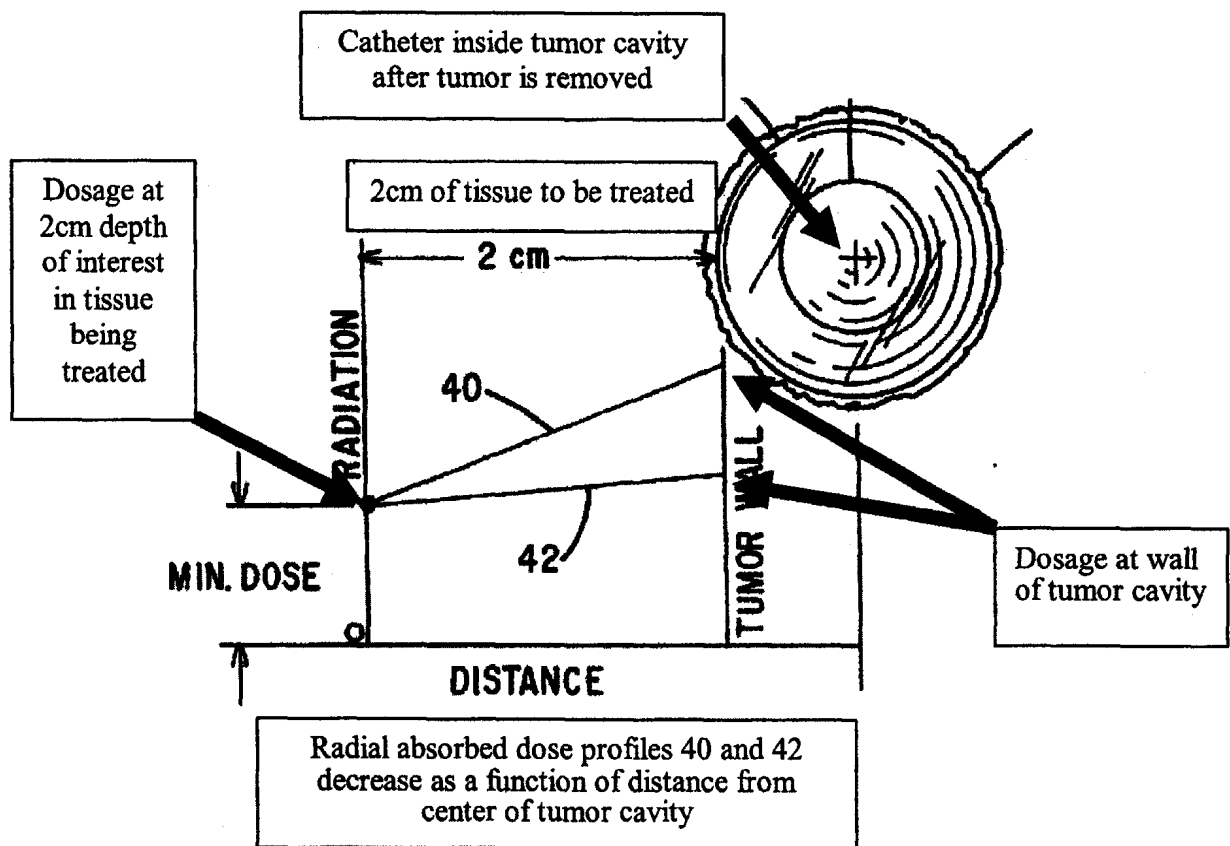
Cytec’s Proposed Construction	Xoft’s Proposed Construction
<i>Disputed Function:</i> Modifying the ratio of the absorbed dose at a depth of interest in the target tissue to the absorbed dose at the surface of the tissue.	<i>Disputed Function:</i> Making the dose along a radius extending from the radionuclide outwardly from the outer chamber wall the same at every point on the radius.
<i>Disputed Structure:</i> A radiation absorbing or attenuating material, e.g., air, x-ray contrast fluid, contrast media used in angiography, water, a gas, or barium sulfite.	<i>Disputed Structure:</i> No such means disclosed in the ‘813 patent, means for making more uniform disclosed as substance within outer chamber.

Because this is a “means-plus-function” limitation subject to 35 U.S.C. § 112, ¶ 6, the Court must construe the limitation’s function as well as the structure disclosed in the specification that corresponds to that function. *BBA Nonwovens Simpsonville, Inc. v. Superior Nonwovens, L.L.C.*, 303 F.3d 1332, 1343 (Fed. Cir. 2002) (Construction of a means-plus-function limitation “requires the court to first identify the function of the means-plus-function limitation and next identify the corresponding structure in the written description necessary to perform that function.”). The function required by this limitation is “rendering uniform the radial absorbed dose profile of the emissions.” As Dr. Verhey explains, the radial absorbed dose profile is defined as the absorbed dose in tissue, varying as a function of distance from the center of the cavity along a particular direction of interest. (Verhey Rep. at 6:21-23.) In the ‘813 patent, the direction of interest would be from the wall of the surgical cavity to a depth in the target tissue at which a prescribed therapeutic dose is defined. (*Id.*) These profiles are shown as lines 40 and 42 in the ‘813 patent at Figure 4, reproduced on the next page and annotated for discussion purposes:

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The patentees have defined in the specification what they mean by “rendering uniform the radial absorbed dose profile of the emissions.” *Phillips*, 415 F.3d at 1316 (claims must be read in light of the specification). In Figure 4, line 40 is a plot of the absorbed dose as a function of radial distance that would be obtained if there were no structure defining an inner volume, *i.e.*, if the entire spherical volume of the tumor were completely filled with radioactive fluid. (Col. 3:20-24.) Plot 42, by contrast, shows the absorbed dose as a function of radial distance when the radioactive fluid is contained within an inner volume (defined by a polymeric film wall) and is surrounded by a radiation absorbing material contained in the outer volume. (Col. 3:24-28.) According to the specification, “[c]omparing plots 40 and 42, by providing the concentric arrangement depicted, the absorbed dose profile in the space between the 2cm site and the wall of the outer balloon is maintained *much more uniform*, thus preventing over-treatment of body tissue at or close to the outer wall 36 of the instrument.” (Col. 3:28-33 (emphasis added).) As Dr. Verhey explains, plot 42 in Figure 4 shows a smaller ratio of the absorbed dose at the wall of the tumor cavity to the dose at the 2cm depth of interest than plot 40. Thus, as the specification defines the term, “rendering uniform the radial

1 absorbed dose profile of the emissions” means modifying the ratio of the absorbed dose at a depth of
2 interest in the target tissue to the dose at the surface of the tissue, as exemplified by the difference
3 between the slopes of plots 40 and 42.

4 Xoft’s construction of this function is unreasonable because it excludes the preferred
5 embodiments shown in the specification. “A claim construction that excludes a preferred embodiment
6 . . . is ‘rarely, if ever, correct.’” *Pfizer, Inc. v. Teva Pharms. USA, Inc.*, 429 F.3d 1364, 1374 (Fed. Cir.
7 2005) (quoting *SanDisk Corp. v. Memorex Prods., Inc.*, 415 F.3d 1278, 1285 (Fed. Cir. 2005));
8 *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996) (same). In the diagram in
9 Figure 4, the radial absorbed dose profile plot 42 does not show the same dose at every point along the
10 radius, as Xoft would require. Rather, the ratio of the dose at the cavity wall to the dose at the depth of
11 interest is less than that for the configuration in plot 40, consistent with Cytyc’s construction.

12 The corresponding structure disclosed in the specification for performing this function is a
13 radiation absorbing or attenuating material, *e.g.*, air, x-ray contrast fluid, contrast media used in
14 angiography, water, a gas, or barium sulfite. *Kahn*, 135 F.3d at 1476 (holding that structure described
15 in the specification is corresponding structure if the specification “clearly links or associates that
16 structure to the function recited in the claim.”). Xoft appears to agree, suggesting that the “substance
17 within the outer chamber” corresponds to the function for making the radial absorbed dose profile
18 more uniform.

19 **G. “The Radioactive Material” (Claim 8)**

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
The material of claim 1 containing a radionuclide.	Indefinite because no antecedent.

24 Again, Xoft offers no construction of this term, arguing only that it is indefinite. Xoft’s
25 argument fails. Claim 8 depends from claim 1, and it is obvious that the “the radioactive material” in
26 claim 8 clearly refers back to “a material containing a radionuclide” described in claim 1, given that
27 the “radionuclide” is the only radioactive material mentioned in claim 1. Anyone skilled in the art
28

1 would know that the “radioactive material” in claim 8 refers to the “material containing a radionuclide”
2 in claim 1. Claim 8 is therefore not indefinite.

3 **H. “A Plurality Of Radioactive Solid Particles Placed At Pre-determined**
4 **Locations Within The Inner Spatial Volume To Provide A Desired**
5 **Composite Radiation Profile” (Claim 12)**

Cytac’s Proposed Construction	Xoft’s Proposed Construction
A plurality of radioactive solid particles placed at pre-determined locations within the inner spatial volume to provide a desired dose profile that is the sum of the radiation profiles of the plurality of particles.	Static array of solid radioactive particles each placed in a single location and mounted on distal ends of separate wires. “Desired composite radiation profile” is indefinite.

10 Xoft’s proposed construction of this term improperly imports limitations from the specification
11 that are merely examples of the preferred embodiment. The ordinary meaning of this claim term,
12 which Cytac proposes as the proper construction here, follows the language of the claim: “A plurality
13 of radioactive solid particles placed at pre-determined locations within the inner spatial volume to
14 provide a desired dose profile that is the sum of the radiation profiles of the plurality of particles.”
15 (See AHC at 286 (defining composite as “made up of distinct components; compound”).)

16 **II. TERMS IN THE ‘204 PATENT**

17 The ‘204 patent, which is a continuation-in-part of the ‘813 patent, describes an apparatus for
18 brachytherapy and a method of using it for interstitial delivery of radiation to diseased cells within the
19 interstices of the tissue surrounding the cavity created by the surgical removal of proliferative tissue.
20 The apparatus includes a catheter body member having a proximal end and a distal end, an inner
21 spatial volume proximate to the distal end of the catheter body member, an outer spatial volume
22 defined by an expandable surface element proximate to the distal end of the body member, and
23 surrounding and concentric with the inner spatial volume. In a preferred embodiment, a radiation
24 source is disposed within the inner spatial volume.

25 The ‘204 patent describes a number of embodiments that can be used in the apparatus for
26 delivering a therapeutic dose of radiation, including, without limitation, radioactive microspheres (FIG.
27 4), concentric non-spherical chambers (FIG. 5), a single solid radiation emitting material surrounded
28 by an expandable cage defining the shape of the tumor cavity (FIG. 6), a radioactive fluid filling the

1 outer chamber (FIG. 7a), a radioactive fluid filling the inner chamber and the outer chamber filled with
2 air or other radiation absorbing substance (FIG. 7b), and a single solid source surrounded by an outer
3 chamber filled with a radiation absorbing substance (FIG. 7c). Figure 7d shows examples of radiation
4 profiles which might be obtained by the embodiments shown in Fig. 7a-7c where the depth of interest
5 is shown as 2cm from the surface of the outer volume. As can be seen, different embodiments can be
6 used to vary the ratio of the dose at the prescribed depth to the dose at the wall of the cavity.

7 **A. "Interstitial" (All Asserted Claims)**

Cytac's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Site in natural or surgically created cavity in body.

12 Cytac addresses the construction of this term in connection with its construction of the term
13 "interstitial brachytherapy" below. Cytac believes that a separate construction of this term divorced
14 from the context of the surrounding claim language is neither required nor appropriate. *See Phillips*,
15 415 F.3d at 1314.

16 **B. "Brachytherapy" (All Asserted Claims)**

Cytac's Proposed Construction	Xoft's Proposed Construction
Radiation therapy delivered by a spatially confined radiation source at or near the site of the diseased tissue.	Radiation therapy delivered by a spatially confined radionuclide at or near a tumor or other proliferative tissue disease site.

21 The parties mostly agree on the definition of "brachytherapy" with two exceptions. *First*, Xoft
22 attempts to limit brachytherapy to the use of a "radionuclide" for irradiating tissue. But radiation can
23 be provided from sources that are not radionuclides (but that can be equivalent to radionuclides), *e.g.*
24 an X-ray tube. (*See Exhibit F to the Declaration of Henry C. Su (The Physics of Radiation Therapy)* at
25 418 ("Brachytherapy is a method of treatment in which sealed radioactive sources are used to deliver
26 radiation at a short distance by interstitial, intracavitary, or surface application.")) There is no reason
27 to limit brachytherapy to use of a radionuclide and Xoft's construction should be rejected. *Second*,
28 Xoft improperly attempts to limit brachytherapy to treatment of tumors or other proliferative tissue

diseases. But there is no basis for such a limitation, as radiation can be applied to any diseased tissue as a doctor believes appropriate.

C. “Interstitial Brachytherapy” (All Asserted Claims)

Cytac’s Proposed Construction	Xoft’s Proposed Construction
Brachytherapy applied directly to the interspaces of a body tissue, where the interspaces are not naturally occurring.	Radiation therapy delivered by a spatially confined radionuclide at or near a tumor site in a natural or surgically resected cavity in a body.

Xoft has, for almost all the other disputed terms in the ‘204 patent, improperly added limitations that are not supported by the terms’ plain meaning or the patent specification or prosecution history. With respect to “interstitial brachytherapy,” which the inventors specifically defined in the prosecution history as excluding certain types of therapies, Xoft now improperly redefines the term in a manner inconsistent with the inventors’ clear statements. Xoft may not blithely ignore the intrinsic evidence.

Specifically, Xoft’s attempt to include “natural” body cavities in its definition of “interstitial brachytherapy” is directly contrary to the patent’s prosecution history. During prosecution of the ‘204 patent, in traversing a rejection from the examiner, the inventors distinguished between brachytherapy applied to a natural body cavity and interstitial brachytherapy:

Turning to the cited prior art, the Ishiwara device comprises a thermotherapeutic apparatus having a catheter body member, an inner lumen surrounded by an outer lumen, and a radiation source contained within the inner lumen. As disclosed in col. 4, lines 19-23, Ishiwara’s apparatus is inserted into a body cavity. . . . Hence the apparatus does not provide *interstitial* radiation treatment, as Applicant’s invention requires, but rather intercavitary radiation treatment.

(Exhibit E to the Declaration of Henry C. Su (12/20/00 Amendment and Response (“Amendment”)) at 11 (emphasis in original; internal citations omitted).)

Similarly, with respect to another reference, the inventors distinguished intraluminal therapy from interstitial therapy:

Weinberger discloses in Figure 17 an intercavitary radiotherapy device for insertion within a patient’s lumen. . . . Like Ishiwara, Weinberger’s apparatus does not provide *interstitial* radiation treatment, as Applicant’s invention requires, but instead *intraluminal* radiation treatment. Whereas Applicant’s device treats disease that is

embedded in tissue (e.g., breast cancer), Ishiwara and Weinberger treat disease in a luminal cavity. For this reason, in Ishiwara and Weinberger, the catheters and expandable balloons are very different than those of Applicant's invention.

(Amendment at 12 (emphasis in original; internal citations omitted).) In light of these clear statements, Cytyc is surprised that Xoft would even attempt to propose a construction of "interstitial brachytherapy" that included natural body cavities or lumens.

In summary, the inventors have specifically excluded "intercavitary" or "intraluminal" radiation therapy – i.e., insertion of a brachytherapy apparatus within a natural body cavity or lumen – from the definition of "interstitial brachytherapy." Cytyc's proposed construction comports with the plain meaning of the claim term, based on the inventors' disclaimer in the prosecution history.

D. "Inner Spatial Volume" (All Asserted Claims)

Cytyc's Proposed Construction	Xoft's Proposed Construction
A region of space surrounded by an outer spatial volume that is defined by an expandable surface element.	Inner balloon in two-balloon device or spherical solid radionuclide in one-balloon device.

Xoft's attempt to limit the "inner spatial volume" to a "balloon" or a "spherical solid radionuclide" should be rejected. A "balloon" is not even one of the embodiments of the "inner spatial volume" described in the specification. Rather, as in the '813 patent, the specification of the '204 patent describes, as an exemplary embodiment, that "the inner spatial volume 30 . . . *may* be defined by a generally spherical polymeric film wall 32." (Col. 3:58-59.) In any event, it is improper to limit the claim language to the embodiments in the specification, as Xoft proposes. *Phillips*, 415 F.3d at 1323 (one must "avoid the danger of reading limitations from the specification into the claim.").

More fundamentally, Xoft continues to confuse the structure that defines an inner spatial volume with the volume itself. The specification provides that the inner spatial volume 30 "may be defined by a generally spherical polymeric film." The film defines the boundary of the volume but the volume is the region of space within that boundary. Thus, according to the specification, the inner spatial volume is simply a region of space surrounded by an outer spatial volume. (See col. 2:39-45 ("The apparatus includes . . . an inner spatial volume disposed proximate to the distal end of the catheter body member, [and] an outer spatial volume defined by an expandable surface element

1 disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial
2 volume”).)

3 Cytyc’s proposed construction fully captures the plain meaning of “inner spatial volume,”
4 which the Federal Circuit notes is of “primary importance” in claim construction. *Phillips*, 415 F.3d
5 1312. A “spatial volume” is a commonly understood English term, meaning “a region of space.”
6 (AHC at 1513 (defining “volume” as “the amount of space occupied by a three-dimensional object or
7 region of space, expressed in cubic units”).) The word “inner” means that that region of space is
8 located within something else, and the specification provides that that “something else” is another
9 (outer) “spatial volume.” (Col. 1:52-55.) Thus, “inner spatial volume” should be construed to mean “a
10 region of space surrounded by an outer spatial volume that is defined by a closed inflatable chamber.”

11 **E. “Outer Spatial Volume” (All Asserted Claims)**

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
<p>No construction required or appropriate.</p> <p>Alternatively: a region of space defined by an expandable surface element and surrounding an inner spatial volume.</p>	<p>Balloon or cage.</p>

17 Cytyc believes that no construction of this term is required or appropriate. The term has its
18 ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic
19 evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning
20 to the term. Thus, “outer spatial volume” should be construed to mean “outer spatial volume.”

21 Xoft’s proposed construction of the term, like its proposed construction of “inner spatial
22 volume,” confuses the outer spatial volume with the “expandable surface element” that defines its
23 boundary. The “outer spatial volume” is a region of space that is *defined* by an “expandable surface
24 element” but it is not the “expandable surface element” itself. (See col. 3:61-65.) If the Court is
25 inclined to construe “outer spatial volume,” then the term should be construed as “a region of space
26 defined by an expandable surface element and surrounding an inner spatial volume.” This is consistent
27 with the ordinary meaning of the claim term in view of the specification.
28

F. "Expandable Surface Element" (All Asserted Claims)

Cytec's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate. Alternatively: a device that can be expanded or inflated, such as an expandable cage or an inflatable balloon.	Deflated balloon or collapsed cage.

Cytec believes that no construction of this term is required or appropriate. The term has its ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning to the term. "Expandable surface element" should be construed to mean "expandable surface element."

Xoft's attempt to limit the term to a "deflated balloon or a collapsed cage" is improper, and there is no support for doing so in any of the intrinsic evidence. Something that is "expandable" is capable of expansion (or inflation) and can be in any state of expansion (or inflation) from no expansion to full expansion. Indeed, as Dr. Verhey explains, a person having ordinary skill in the art would expect to have to expand the expandable surface element in order to practice the invention of the '204 patent. (Verhey Rep. at 9:17-20, 10:16-18.) A construction that limits this element to a "deflated" or "collapsed" state is unreasonable and erroneous.

G. "Radiation Source" (All Asserted Claims)

Cytec's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Radionuclide

Cytec believes that no construction of this term is required or appropriate. The term has its ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning to the term. A "radiation source" is simply that—a radiation source. Xoft's attempt to limit a "radiation source" to just radionuclides, a specific kind of source, is unsupportable.

H. “Minimum Prescribed Dose” (Claims 2, 18, 24, 32, & 36)

Cytec’s Proposed Construction	Xoft’s Proposed Construction
Minimum prescribed dose received within a target tissue for delivering therapeutic effects.	Minimum dose needed to treat cancer cells.

Xoft’s attempt to limit this term to the provision of a dose to treat cancer cells is improper and unsupported. The term has its ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning to the term. The meaning can be readily discerned from the context of the surrounding claim language – “a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue.” (*See, e.g.*, col. 8:31-33.) *See also Phillips*, 415 F.3d at 1314 (“Quite apart from the written description and the prosecution history, the claims themselves provide substantial guidance as to the meaning of particular claim terms. . . . To begin with, the context in which a term is used in the asserted claim can be highly instructive.”)

I. “Delivering A Prescribed Absorbed Dose” (Claim 34)

Cytec’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Indefinite – the patent contains no information on how to obtain a prescribed dose, much less a prescribed dose using an expandable surface element.

Cytec believes that no construction of this term is required or appropriate. The term has its ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning to the term. Contrary to Xoft’s assertion, the phrase is not indefinite because a “prescribed absorbed dose” refers to the fact that the amount of the dose to be delivered to a target tissue is within the discretion (i.e., prescription) of a person with ordinary skill in the art to determine. For example, a radiation oncologist determines, using treatment planning software or some other reference or tool, the proper dosage for each patient, depending on a number of physiological factors. The patient-specific

1 amount of radiation is a “prescribed dose.” As to how the dose is delivered, Dr. Verhey explains that
2 “once the inflatable expandable surface element is in contact with the surface of the surgical cavity, the
3 dose at the prescription depth can be delivered once the radiation source is introduced into the
4 catheter.” (Verhey Rep. at 9:26-28 (citing col. 5:66 – 6:28).) Delivering a prescribed absorbed dose is
5 not indefinite and the term means exactly what it says—delivering a prescribed absorbed dose.

6 **J. “The Inner And Outer Spatial Volumes Are Configured To Provide A**
7 **Minimum Prescribed Absorbed Dose” (Claim 2 & 36) And “Configuring**
8 **The Inner And Outer Spatial Volumes To Provide A Minimum Prescribed**
9 **Absorbed Dose” (Claims 24 & 32)**

Cytac’s Proposed Construction	Xoft’s Proposed Construction
<p>10 The inner and outer spatial volumes are</p> <p>11 configured to provide a minimum prescribed</p> <p>12 absorbed dose for delivering therapeutic effects</p> <p>13 to a target tissue;</p> <p>14 and</p> <p>15 Configuring the inner and outer spatial</p> <p>16 volumes to provide a minimum prescribed</p> <p>absorbed dose for delivering therapeutic effects</p> <p>to a target tissue.</p>	<p>Indefinite – configured volumes are expanded</p> <p>volumes, but no cause and effect relationship</p> <p>between configuring of inner and outer</p> <p>volumes and providing dose of any prescribed</p> <p>amount.</p>

17 Contrary to Xoft’s contention, this term is not indefinite. The ‘204 patent discloses in detail the
18 various ways in which a person of ordinary skill in the art can achieve a configuration of the inner and
19 outer spatial volumes that will deliver a minimum prescribed dose to a target tissue of interest. (See,
20 e.g., col. 5:22-41; col. 6:16 – col. 7:28.) As Dr. Verhey explains:

21 [W]here the radioactive material is disposed in the inner spatial volume, the rate at
22 which the dose falls off between the surface of the surgical cavity and the depth at
23 which the minimum dose is to be prescribed, can be controlled by modifying the
24 quantity and type of radiation absorbing material contained within the outer spatial
25 volume. The safe delivery of the minimum prescribed dose at the depth of interest
26 requires that the tissue intervening between the surface of the cavity and the depth of
27 interest receive a dose which is equal to or greater than the prescribed dose but less than
28 that which would necrose (i.e., lethally damage) healthy tissue.”

(Verhey Rep. at 8:25 – 9:3.) Because one skilled in the art knows how to configure the spatial
volumes to provide the minimum prescribed absorbed dose, the term is not indefinite.

K. "A Minimum Distance Outward From The Outer Spatial Volume Expandable Surface" (Claims 2, 24, 32, & 36)

Cytec's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Indefinite because it is some unknown distance from deflated balloon or collapsed cage. Patent contains no information regarding determination of minimum distance.

Cytec believes that no construction of this term is required or appropriate and that the term is definite. The term has its ordinary and customary meaning and is understood by one of ordinary skill in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning to the term.

The meaning of "a minimum distance outward from the outer spatial volume expandable surface" is not indefinite and can be readily discerned from the context of the surrounding claim language – "the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface." The disputed phrase refers to the minimum distance outward from the expandable surface element that defines the outer spatial volume. This minimum distance defines the thickness of a layer of target tissue which, in the determination of a person of ordinary skill in the art, includes the region in which diseased cells might reside. (Verhey Rep. at 9:6-9.)

L. "Controlled Dose" (Claim 2, 24, 32, & 36)

Cytec's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Indefinite because configuration, i.e., expansion, of inner and outer volumes does not control dose.

Cytec addresses the construction of this term in connection with its construction of the phrase "providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface" below. Cytec believes that a separate

1 construction of this term divorced from the context of the surrounding claim language is neither
2 required nor appropriate.

3 **M. “To Reduce Or Prevent Necrosis In Healthy Tissue Proximate To The**
4 **Expandable Surface” (Claims 2, 24, 32, & 36)**

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Indefinite – patent does not describe providing a dose through expandable surface – improper functional limitation in apparatus claim.

9 Cytyc addresses the construction of this term in connection with its construction of the phrase
10 “providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent
11 necrosis in healthy tissue proximate to the expandable surface” below. Cytyc believes that a separate
12 construction of this term divorced from the context of the surrounding claim language is neither
13 required nor appropriate.

14 **N. “Providing A Controlled Dose At The Outer Spatial Volume Expandable**
15 **Surface To Reduce Or Prevent Necrosis In Healthy Tissue” (Claims 2, 24,**
16 **32 & 36)**

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
Controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target issue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface	Indefinite because radiation dose is not provided when outer volume surface is “expandable”, i.e., is a deflated balloon or a collapsed cage. Also indefinite because patent contains no information on how to provide dose that will reduce or prevent necrosis in healthy tissue. In context, the word “necrosis” and the term “necrosis in healthy tissue” are indefinite.

23 Xoft does not offer a construction of this disputed term; it only argues that the term is
24 indefinite. But the term is well understood by those of skill in the art. Dr. Verhey explains that by
25 adjusting the distance between the radiation source and the surface of the outer spatial volume, or by
26 adjusting the type of radiation absorbing material in the outer spatial volume, the ratio of the dose at
27 the surface of the outer spatial volume to the prescribed dose at the depth of prescription can be
28

controlled. (Verhey Rep. at 9:12-15.) The dose must not be so high that it causes necrosis to occur in healthy tissue that is in contact with the expandable surface; persons of skill in the art will know how high such a dose may be before a significant percentage of healthy cells necrose. (*Id.*)

O. “Adapting The Expandable Surface To Contact Tissue Surrounding The Resection Cavity To Conform The Tissue” (Claim 34)

Cytec’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Indefinite because expandable surface, i.e., deflated balloon or collapsed cage, neither contacts nor conforms the tissue surrounding the resection cavity. The patent contains no information on how this could be done.

Cytec believes that no construction of this term is required or appropriate and that the term is definite. The term has its ordinary and customary meaning and is understood by one of ordinary skill in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning to the term. The term “adapting the expandable surface to contact tissue surrounding the resection cavity to conform the tissue to the desired shape of the expandable surface element” means adapting the expandable surface so that it comes into contact with the tissue forming the wall of the resection cavity and conforms that tissue to its shape. This comports with the ordinary meaning of the claim term.

Xoft’s indefiniteness assertion is premised on its flawed construction of “expandable surface,” which requires that the surface be in a deflated or collapsed state. The fact that claim 34, however, requires the expandable surface to contact the tissue surrounding the resection cavity establishes that Xoft’s construction of “expandable surface” is erroneous. Under a proper construction, the expandable surface can be inflated or expanded to some degree so that it contacts the tissue and conforms the tissue to its shape. Dr. Verhey explains: “the volume of the expandable surface can be adjusted by inflation until the surface of the expandable volume is in contact with the surface of the resection cavity at all points. In this state, the shape of the resection cavity conforms to the shape of the expandable surface.” (Verhey Rep. at 9:18-20 (citing col. 5:47-61).)

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P. “Desired Shape Of The Expandable Surface Element” (Claims 4, 26, & 34)

Cytc’s Proposed Construction	Xoft’s Proposed Construction
The desired shape of the expandable surface element.	Indefinite. Patent contains no information regarding the desired shape of an expandable surface element, i.e., a deflated balloon or collapsed cage.

Cytc believes that no construction of this term is required or appropriate and that the term is definite. The term has its ordinary and customary meaning and is understood by one of ordinary skill in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning to the term.

This term is not indefinite, as Xoft wrongly contends. The desired shape of the balloon is within the discretion of those skilled in the art. According to Dr. Verhey, “the desired shape of the expandable surface element is that shape which provides the predetermined constant spacing between the inner spatial volume and the conformed surface of the resection cavity.” (Verhey Rep. at 9:22-24 (citing col. 5:47-61).) Examples of desired shapes described in the specification include a spherical balloon (FIG. 1) and a cylindrical balloon (FIG. 5), but the invention is not limited to any particular shape. (Col. 5:13-16.)

Q. “Predetermined Spacing” (Claims 3 & 25)

Cytc’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Indefinite because no information in patent re how to determine “predetermined spacing.” Also indefinite because spacing is between inner spatial volume and expandable surface element, i.e., deflated balloon or collapsed cage.

Cytc addresses the construction of this term in connection with its construction of the phrase “a predetermined spacing is provided between said inner spatial volume and the expandable surface element” below. Cytc believes that a separate construction of this term divorced from the context of the surrounding claim language is neither required nor appropriate.

R. “A Predetermined Spacing Is Provided Between Said Inner Spatial Volume And The Expandable Surface Element”/ “A Predetermined Spacing Between Said Inner Spatial Volume And The Expandable Surface Element” (Claims 3 & 25)

Cytec’s Proposed Construction	Xoft’s Proposed Construction
The distance between the inner spatial volume and the expandable surface element is determined in advance.	A predetermined spacing between inner spatial volume and deflated balloon or collapsed cage is indefinite.

Cytec believes that no construction of this term is required or appropriate and that the term is definite. The term has its ordinary and customary meaning and is understood by one of ordinary skill in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning to the term.

Contrary to Xoft’s assertion, the term is not indefinite and has an ordinary and customary meaning to one skilled in the art. Dr. Verhey readily understood the term to mean that the spacing between the inner and outer volumes can be set to a predetermined value by modifying the level of inflation or expansion of one or both volumes. Although Xoft incorrectly suggests that the patent must describe that amount of spacing, a patent does not need to describe what one skilled in the art already knows and can practice. *See S3 Inc. v. nVidia Corp.*, 259 F.3d 1364, 1371 (Fed. Cir. 2001). One skilled in the art knows how to determine an appropriate “predetermined spacing.”

Moreover, to the extent Xoft contends that there can be no spacing between the inner volume and a deflated balloon or collapsed cage, that argument also fails. Such an argument is premised on the erroneous proposal that “expandable surface” be limited to a deflated or collapsed surface. Because that construction is inconsistent with the patent and must be rejected for the reasons set forth above (*see supra* at II.F), Xoft’s indefiniteness argument must also fail.

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S. "Intraoperatively" (Claims 19 & 34)

Cytec's Proposed Construction	Xoft's Proposed Construction
Intraoperatively Alternatively: during the surgical operation to remove proliferative tissue	After surgical removal of tumor but prior to closing the surgical site.

The parties appear to agree for the most part as to the meaning of "intraoperatively," and Cytec could agree to Xoft's proposed construction if only the construction does not include "closing the surgical site," which is superfluous. "Intraoperatively" simply means during the surgical operation to remove the proliferative tissue. Whether the site is subsequently closed (*e.g.*, with sutures) is irrelevant.

T. "Solid Radiation Source" (Claim 16)

Cytec's Proposed Construction	Xoft's Proposed Construction
A radiation source that has a fixed shape and volume, and is not deformable.	Solid radionuclide

Xoft again improperly attempts to limit a radiation source to a radionuclide. There are other sources of radiation besides radionuclides, and there is no basis in the intrinsic evidence for limiting the plain meaning of "radiation source" to a radionuclide. Moreover, Xoft neglects to define "solid," which refers to the fact that the radiation source that has a fixed shape and volume and is not deformable. (*See* AHC at 1295 ("of definite shape and volume; not liquid or gaseous"); Verhey Rep. at 11:8-9.)

U. "The Prescribed Absorbed Dose Is Delivered To The Target Tissue In Substantially Three Dimensions" (Claim 18)

Cytec's Proposed Construction	Xoft's Proposed Construction
The prescribed absorbed dose is delivered to the target tissue such that all points at a given outward distance from the tissue wall will receive the same dose.	Prescribed absorbed dose is indefinite and substantially three dimensional is indefinite.

1 Contrary to Xoft's assertion, there is nothing indefinite about this limitation because one of
2 ordinary skill in the art would understand what a prescribed absorbed dose is and how that dose can be
3 delivered substantially in three dimensions. Dr. Verhey explains that this limitation relates to the fact
4 that, once the outer chamber is expanded, the tissue in contact with the chamber conforms to the shape
5 of the chamber, thereby assuring that all points within the tissue that are at a fixed distance from the
6 wall of the surgical cavity will receive the identical dose. (Verhey Rep. at 11:12-15.) In this manner,
7 the prescribed dose is delivered to the target tissue at the depth of interest substantially in all three
8 dimensions, as opposed to being delivered in only two dimensions (to all points on a plane) or one
9 dimension (to all points along a line). The limitation is clear, not indefinite, and should be given its
10 ordinary meaning.

11 **CONCLUSION**

12 For the reasons stated above, this Court should adopt Cytyc's proposed constructions of the
13 disputed terms of the '813 and '204 patents, and reject Xoft's proposed constructions and
14 indefiniteness arguments.

15 Respectfully submitted,

16 DATED: November 9, 2006

17 HOWREY LLP

18
19 By: /s/ Henry C. Su
20 Henry C. Su

21 Attorneys for Defendants CYTYC CORPORATION and
22 CYTYC SURGICAL PRODUCTS II, INC.
23
24
25
26
27
28

CERTIFICATE OF SERVICE

As required by Civil Local Rule 5-6(a)(2), the undersigned hereby certifies that on November 9, 2006, a true and correct copy of:

**DEFENDANT AND COUNTERCLAIMANT CYTYC CORPORATION'S
OPENING CLAIM CONSTRUCTION BRIEF (PAT. L.R. 4-5(a))**

was served on the following counsel of record for Xoft, Inc. electronically through this Court's Electronic Case Filing System, in accordance with Civil Local Rule 5-5(b):

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/s/ Henry C. Su
Henry C. Su

Exhibit 7

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

XOFT MICROTUBE, INC.,)
)
 PLAINTIFF,)
)
 VS.)
)
CYTYC CORPORATION AND)
PROXIMA THERAPEUTICS, INC.)
)
 DEFENDANTS.)

)

TRANSCRIPT OF PROCEEDINGS
BEFORE THE HONORABLE RONALD M. WHYTE
UNITED STATES DISTRICT JUDGE

A P P E A R A N C E S:

FOR THE PLAINTIFF: ORRICK, HERRINGTON & SUTCLIFFE
BY: JAMES W. GERIAK,
KURT T. MULVILLE, AND
MARK A. STIRRAT
4 PARK PLAZA, SUITE 1600
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FOR THE DEFENDANT: HOWREY, SIMON, ARNOLD & WHITE
BY: MATTHEW M. WOLF
1299 PENNSYLVANIE AVENUE, NW
WASHINGTON, DC 20004

BY: HENRY C. SU AND
MARK COHEN
1950 UNIVERSITY AVENUE, 4TH FLOOR
EAST PALO ALTO, CALIFORNIA 94303

OFFICIAL COURT REPORTER: LEE-ANNE SHORTRIDGE, CSR, CRR
CERTIFICATE NUMBER 9595

1 THE COURT: OKAY.

2 MR. GERIAK: IF I MIGHT, YOUR HONOR, ONE
3 LAST COMMENT.

4 THE CLAIM UPON WHICH CLAIM 12 DEPENDS,
5 NAMELY, CLAIM 1, SAYS THAT THERE HAS TO BE A
6 CONSTANT SPACING BETWEEN THE RADIOACTIVE MATERIAL
7 AND THE OUTER WALL IN ORDER FOR THIS DEVICE TO BE
8 WHAT THEY WANT IT TO BE.

9 AND BESIDES THAT, HERE, IF YOU LOOK AT
10 FIGURE 5 OF THE '813 PATENT, THOSE BLACK DOTS ARE
11 THE RADIATION, RADIONUCLIDES, AND EACH ONE OF THEM
12 IS AN UNEQUAL DISTANCE, A NONCONSTANT DISTANCE FROM
13 THE WALL.

14 THEY'RE EACH CLOSER TO ONE AREA OF THE
15 WALL AND FURTHER FROM ANOTHER AREA OF THE WALL.

16 AND THE CLAIM ATTEMPTS TO SOLVE THIS
17 PROBLEM WITH THE IMAGINARY LINE, AND IT SAYS -- IT
18 SAYS, OKAY, IN EFFECT, THE $1 \text{ OVER } R \text{ SQUARED}$ THAT
19 APPLIES TO EACH OF THESE POINTS IS DIFFERENT.

20 BUT I'LL TRY TO MAKE THAT GO AWAY BY
21 SAYING I'VE GOT AN INNER SPACIAL VOLUME DEFINED BY
22 AN IMAGINARY LINE, AND THAT INNER SPACIAL VOLUME IS
23 A CONSTANT DISTANCE AWAY FROM THE WALL OF THE
24 BALLOON.

25 SO THIS IS -- THIS IS JUST NOT A CLAIM

1 THAT MAKES ANY SENSE.

2 THE COURT: HOW DO YOU HAVE CONSTANT
3 SPACING IF YOU HAVE MORE THAN ONE NUCLIDE PARTICLE?

4 MR. WOLF: YOUR HONOR, YOU'LL RECALL
5 DR. VERHEY PUT UP THE GRAPH OF THE MULTIPLE
6 CATHETERS IN THE TREATING PROSTATE CANCER.

7 THE COURT: UM-HUM.

8 MR. WOLF: AND THERE WERE ACTUAL PHYSICAL
9 CHARTS SHOWING THE SHAPE, THE DOSE THAT CREATED. I
10 CAN BRING IT -- CALL IT BACK UP IF YOU'D PREFER.

11 THE COURT: MAYBE YOU SHOULD.

12 MR. WOLF: DO YOU -- PERHAPS CAN WE
13 SUBMIT DR. VERHEY'S CHART JUST AFTER THE FACT AND
14 THAT MIGHT HELP YOU IN YOUR CONSIDERATION, OR --
15 WE'D HAVE TO SWAP COMPUTERS, WHICH WE CAN DO IF
16 YOU'D LIKE TO SEE IT.

17 THE COURT: I'M JUST NOT RECALLING
18 EXACTLY WHAT YOU'RE TALKING ABOUT.

19 MR. WOLF: SURE. THERE WERE IMAGES OF --
20 REMEMBER, THERE WAS CONCENTRIC CIRCLES OF DOSE
21 LEVELS, DIFFERENT COLORS, AND DR. VERHEY SAID HE
22 COULDN'T READ THE EXACT NUMBERS, BUT THERE WAS RED
23 AND BLUE AND -- THAT -- THE MULTIPLE SOURCES
24 CREATED A DOSE, AND THE QUESTION IS, IF IT'S A
25 CIRCLE, IS IT CONSTANT COMPARED TO THE OUTER

1 PROFILE?

2 IF IT IS, YOU'RE WITHIN THE CLAIM.

3 IF IT'S NOT CONSTANTLY SPACED, IF IT'S,

4 FOR EXAMPLE, AN OBLONG FIGURE IN A SPHERICAL

5 BALLOON, THEN YOU DON'T HAVE A CONSTANT DISTANCE.

6 SO IT'S BASED ON THE COMPOSITE DOSE

7 PROVIDE FILE THAT DR. LOVOI TESTIFIED HE UNDERSTOOD

8 WHAT IT WAS.

9 IF THIS COMPOSITE DOSE PROFILE, IN THE

10 REAL WORLD, AS A MATTER OF PHYSICS, CREATES A

11 CIRCULAR DOSE THAT IS CONSTANTLY SPACED FROM THE

12 BALLOON THAT'S SURROUNDING IT, THEN YOU'RE WITHIN

13 THE CLAIM.

14 IF IT DOESN'T, YOU DON'T.

15 MR. GERIAK: YOUR HONOR, THIS IS WAY OFF

16 THE MARK. WHAT MR. WOLF IS SAYING IS THAT THE

17 ISODOSE PROFILE OUTSIDE THE BALLOON IS UNIFORM WITH

18 RESPECT TO THE BALLOON.

19 THAT'S NOT WHAT THE CLAIM IS TALKING

20 ABOUT.

21 MR. WOLF: THE CIRCLE HE DREW WAS THE

22 OUTER CIRCLE. THE INNER CIRCLE -- AGAIN,

23 DR. VERHEY, WOULD YOU LIKE -- WOULD IT BE HELPFUL

24 TO HAVE EXPERT TESTIMONY?

25 THE COURT: SURE.

1 MR. WOLF: I, FRANKLY, THINK THIS IS A
2 BIT OF PILLOW FIGHT CONCERNING THE PRODUCT AT
3 ISSUE, BUT IF WE WANT TO TAKE TIME, WE CAN DO SO.

4 DR. VERHEY: YOUR HONOR, I GUESS MY
5 ANSWER TO WHAT I THINK THE QUESTION IS, IS A RAY OF
6 SPECIFIC PARTICLES, RADIOACTIVE PARTICLES ANY
7 DIFFERENT THAN AN INNER BALLOON FILLED WITH
8 RADIOACTIVE PARTICLES, AND I WOULD SAY NO, IT'S NOT
9 ANY DIFFERENT.

10 THERE'S A CENTER OF GRAVITY OF THAT
11 DISTRIBUTION OF SOURCES WHICH CAN BE CONSIDERED
12 CLOSE TO A POINT, AND WE KNOW HOW TO MAKE
13 CALCULATIONS ABOUT THAT.

14 SO WE CAN ARRANGE THEM IN SUCH A WAY THAT
15 THEY WOULD BE ROUGHLY CONTAINED BY THE IMAGINARY
16 SPHERICAL VOLUME, AND THAT THE DOSE WOULD BE
17 UNIFORM ALONG ANY AXIS THAT CUT THROUGH THE SURFACE
18 OF THE, OF THE CAVITY, WHICH IS WHAT WE'RE
19 INTENDING.

20 MR. GERIAK: A QUESTION, YOUR HONOR.

21 THE COURT: YEAH.

22 MR. GERIAK: WOULDN'T IT ALSO BE TRUE --
23 DR. VERHEY, IF YOU MOVE TO ONE SIDE SO THE JUDGE
24 CAN SEE -- THAT THE DISTANCE FROM THE RADIOACTIVE
25 SOURCES, RADIOACTIVE MATERIALS TO THE WALL OF THE

1 BALLOON WOULD NOT BE CONSTANT.

2 DR. VERHEY: THAT'S TRUE.

3 IT ALSO WOULDN'T BE CONSTANT IF IT'S
4 FILLED WITH RADIOACTIVE FLUID. EACH POINT IN THAT
5 SPHERE OF FLUID WOULD HAVE A DIFFERENT POINT, A
6 DIFFERENT DISTANCE. BUT THE OVERALL EFFECT WOULD
7 BE TO PROVIDE A UNIFORM DOSE.

8 MR. GERIAK: ALL RIGHT. AND, THEREFORE,
9 ISN'T IT TRUE THAT ONLY THE DRAWING OF THAT
10 IMAGINARY LINE RESULTS IN SOMETHING THAT'S A
11 CONSTANT DISTANCE, IF ONE CHOOSES TO DRAW IT THAT
12 WAY, FROM THE WALL OF THE BALLOON?

13 DR. VERHEY: THE DRAWING OF THE SURFACE
14 WHICH CONTAINS THE DISTRIBUTION OF THE PARTICLES
15 WOULD -- COULD BE MADE TO BE UNIFORM RELATIVE TO
16 THE OUTER SURFACE.

17 BUT, IN FACT, WHAT MATTERS IS THE
18 RESULTING DOSE DISTRIBUTION.

19 MR. GERIAK: I DON'T THINK YOU ANSWERED
20 MY QUESTION, DOCTOR.

21 ISN'T IT TRUE THAT WHEN YOU LOOK -- OR
22 LET'S USE THE PATENT DRAWINGS, BECAUSE MY DEPICTION
23 MAY SOMEHOW GET IN THE WAY.

24 ALL RIGHT. YOU AGREE THAT, IN FIGURE 5,
25 THE DARK SPOTS ARE THE RADIOACTIVE MATERIALS?

Exhibit 8

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 CYTYC SURGICAL PRODUCTS II, INC.

UNITED STATES DISTRICT COURT
 NORTHERN DISTRICT OF CALIFORNIA
 SAN JOSE DIVISION

XOFT MICROTUBE, INC.,

Plaintiff,

vs.

CYTYC CORPORATION and PROXIMA
 THERAPEUTICS, INC.,

Defendants.

) Case No. CV 05-05312 RMW

) **DECLARATION OF LYNN J. VERHEY,**
) **PH.D. IN SUPPORT OF CYTYC**
) **CORPORATION'S PROPOSED**
) **CONSTRUCTION OF CLAIM TERMS,**
) **PHRASES AND CLAUSES**

AND RELATED COUNTERCLAIMS

HOWREY LLP

Declaration of Lynn J. Verhey, Ph.D.
 Case No. C05-05312 RMW

1 My name is Lynn J. Verhey. I am a resident of the state of California and am over the age of
2 18. I am presently employed by the University of California, San Francisco as a Full Professor and
3 serving as Vice-Chair in the Department of Radiation Oncology. I make the following declaration
4 based on my personal knowledge, training and experience, and if called upon to testify, I could and
5 would testify competently to the matters set forth below.

6 **I. INTRODUCTION AND MY EXPERT QUALIFICATIONS**

7 I received my B.A. in Physics from Kalamazoo College, Kalamazoo, Michigan in 1962, and
8 my M.S. and Ph.D. in Physics in 1964 and 1968, respectively, from the University of Illinois, Urbana,
9 Illinois. The subject of my research during my education was on the decays of certain charged
10 particles produced by high energy interactions of protons with Hydrogen and Deuterium.

11 I took a position at UCLA and served as a post-doctoral researcher and Assistant Professor of
12 Physics from 1968-70, doing experiments at Lawrence Berkeley Laboratory and teaching physics to
13 undergraduate physics students. I moved to Harvard University in 1970 as an Assistant Professor,
14 continuing to teach undergraduate physics and perform high energy experiments, this time at Fermi
15 National Accelerator Laboratory in Illinois. In 1975 I took a position as Hospital Radiation Physicist
16 at Massachusetts General Hospital (MGH) with a concurrent continuing position as Assistant Professor
17 at the Harvard Medical School. I then worked with the MGH group to develop and implement proton
18 radiation therapy as an alternative to x-ray therapy. In 1990, I took the position as Chief of the Physics
19 Division and Associate Professor in the Department of Radiation Oncology at UCSF. Since that time,
20 I have continued to serve as Chief of the Physics Division and, in addition, as Vice-Chair of the
21 Department and as a Full Professor.

22 As part of my responsibilities at UCSF, I have mentored numerous graduate and post-graduate
23 students, taught an undergraduate class in the Department of Nuclear Engineering at the University of
24 California, Berkeley (UCB) and graduate classes in the Department of Bioengineering at UCB as well
25 as at UCSF. I have taught medical physics to medical residents at UCSF as well as to physics
26 residents. I have performed research on new methods of delivering radiation to cancer patients and
27 have published over 100 technical papers in this field. I was certified as a therapeutic radiological
28 physicist by the American Board of Radiology in 1982, appointed a fellow of the American

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1 Association of Physicists in Medicine in 2002 and a fellow of the American Society of Therapeutic
2 Radiology and Oncology in 2006.

3 I am a well-recognized expert in methods of delivering radiation to cancer patients, having
4 given numerous scientific lectures at scientific meetings, both nationally and internationally. I am
5 attaching a current copy of my curriculum vitae to this declaration.

6 **II. TOPICS THAT I HAVE BEEN ASKED TO ADDRESS**

7 I have been asked by counsel for Cytoc Corporation and Cytoc Surgical Products, Inc. to
8 provide expert testimony relating to United States Patent Nos. 5,913,813 (the "813 patent") and
9 6,413,204 (the "204 patent"), which are the patents of issue in this lawsuit. The 813 patent describes
10 and claims an invention in the field of a balloon catheter for treatment of proliferative tissue, while the
11 204 patent extends this concept to describe and claim as an invention a method for treatment of
12 proliferative tissue diseases using an interstitial brachytherapy apparatus. These patents describe a
13 catheter which can be used with an array of radiation-producing materials to irradiate the wall of a
14 surgical cavity and a defined thickness of tissue beyond that wall, to doses that can both avoid necrosis
15 of normal tissue and destroy cancer cells that might populate the area. In the case of both the 813 204
16 patents, I have been asked to provide testimony with respect to the knowledge of people of ordinary
17 skill in the relevant art and in particular, at the time the described inventions were made, which I
18 understand to be in the time frame of 1997 to 1999, based on their respective filing dates. I have also
19 been asked to provide an opinion of how one of ordinary skill in the art would interpret elements of the
20 claims of the 813 and 204 patents which cover the inventions at issue. I can also provide testimony on
21 any other background information or technical issue on these patents that the Court may request.

22 **III. INFORMATION CONSIDERED IN FORMING MY OPINIONS**

23 In forming the opinions stated in this declaration, I have reviewed and considered the text of
24 the 813 patent and the patent history associated with the issuance of the patent as well as the text of the
25 204 patent and the history associated with its issuance. I have also considered the preliminary claim
26 construction and identification of extrinsic evidence exchanged by both parties. I have also reviewed
27 information in "The Physics of Radiation Therapy" (2d edition, 1994) by Faiz Khan, PhD, published
28 by Williams and Wilkins. I have not reviewed any written or oral opinions from any expert whom

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Xoft Microtube has retained or may retain in connection with the 813 and 204 patents and I reserve the right to modify my opinions stated in this declaration after having reviewed any such opinion offered by any such expert. I also reserve the right to modify my opinions based on any rulings that the Court might issue in the future relating to these patents.

IV. APPROACH I HAVE USED IN READING THE 813 AND 204 PATENTS AND INTERPRETING THEIR CLAIMS

I understand that the claims of the 813 patent at issue in this lawsuit are claims 1, 2, 3, 4, 8 and 12 found in columns 4, 5 and 6 of the patent. I also understand that the claims of the 204 patent at issue in this lawsuit are claims 1, 2, 3, 4, 8, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26, 30, 32, 34, 35 and 36 found in columns 8, 9, 10, 11 and 12 of the patent. In the case of patent 813, the claims relate specifically to subject matter described in columns 1-4, beginning with a summary of the invention and Figures 1-5, and for patent 204, the claims relate specifically to the discussion in columns 2-8, beginning with a summary of the invention and Figures 1-7. I understand that a patent claim must be interpreted in light of the specification of the invention and the illustrative figures which are intended to describe the invention that is being claimed.

I also understand that a claim is to be interpreted from the standpoint of one of ordinary skill in the art, at the time of the invention, which is approximately when a patent application first describing the invention was filed. Based on the respective filing dates of the patent applications, I understand the relevant time frame to be between 1997 and 1999.

I understand that patents 813 and 204 can be considered to have a "parent-child" relationship. Indeed, many of the claims of 204 specifically relate to the same subject matter described in columns 1-4 and figures 1-5 of patent 813. I understand that the proper interpretation of the claims of the 813 and 204 patents also requires analyzing the prosecution history of these two patents, i.e., the public record of the communications exchanged between the applicants and the United States Patent and Trademark Office (PTO) leading up to the issuance of the 813 and 204 patents, respectively.

In understanding and interpreting the claims of the 813 and 204 patents, I have focused on the specifications and drawing figures in the patents, and the prosecution histories of the 813 and 204 patents. I have read these materials as one of ordinary skill in the art would have read them in the

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1 period 1997 to 1999. When appropriate, I have consulted a contemporary reference textbook, which
2 can be helpful in understanding the meaning of a claim term, particularly if the meaning remains
3 unclear after reading the specifications and the prosecution histories.

4 I understand that claim terms are normally used consistently throughout a patent. One has to
5 assign meaning to each and every term in a claim.

6 **V. LEVEL OF SKILL OF ONE OF ORDINARY SKILL IN THE ART**

7 For purposes of interpreting the claims of the 813 and 204 patents, the relevant scientific area is
8 radiation oncology physics, with a focus on brachytherapy. Typically, individuals of ordinary skill in
9 this field would hold a M.S. degree in Physics or Engineering, with 3 or more years of clinical medical
10 physics experience; or a Ph.D. degree in Physics or Medical Physics with 2 or more years of clinical
11 experience.

12 Such a person would have a broad knowledge of the physics of brachytherapy procedures, of
13 the principles of radioactivity and an understanding of the effects of radiation on cells. In addition,
14 such a person would have an understanding of other means of treating cancer cells with radiation such
15 as an external, gantry-mounted linear accelerator. Individuals with such qualifications are considered
16 eligible for certification as a radiation oncology physicist by entities such as the American Board of
17 Radiology and considered capable of working independently in a clinical environment as a medical
18 physicist.

19 **VI. OVERVIEW OF THE INVENTIONS DESCRIBED IN THE 813 AND 204 PATENTS**

20 The claims of the 813 patent relate to the description of an instrument comprising a concentric
21 arrangement of an inner spatial volume and an outer spatial volume defined by an inflatable chamber,
22 disposed near the distal end of a catheter body where one of the volumes can contain a source of
23 radiation, while the other volume would normally contain a radiation absorptive material. In the
24 preferred embodiment, shown in Figure 1 of the patent, the inner volume is an inflatable chamber
25 concentric with the catheter body containing a radioactive source. The outer chamber, concentric with
26 the inner volume, is then inflated with air or other radiation absorbing material, resulting in the wall of
27 the outer chamber being in contact with the outer surface of the surgical cavity at all points. The
28 distance between the radiation source and the wall of the outer chamber can be made constant. This

embodiment permits the delivery of radiation to a ring of tissue outside a surgical cavity that is judged to possibly include cancer cells, and by manipulating the volume and material in the outer chamber, the ratio of the dose to the surface of the surgical cavity to the dose at the tissue depth where the minimum dose is prescribed to be received, can be controlled to maximize the effectiveness of the treatment. An effective treatment could be defined as one that delivers the prescribed dose to the tissue at the depth of interest, and a dose to tissue between the wall of the surgical cavity and the prescription depth which is higher, but not likely to necrose healthy tissue.

The 813 patent teaches that other embodiments can be used to deliver radiation to proliferative tissue outside a surgical cavity and these are discussed in 2:64 – 4:20 and supported by figures 3-5. These other embodiments include the use of a radioactive liquid in an inner inflatable chamber, or a plurality of radioactive solid particles, a slurry of a fluid containing particles of a radioactive isotope or a solid radioactive source. In addition, these same radioactive sources can be placed in the space between the inner inflatable chamber and the outer inflatable chamber. Any of these embodiments might be used as a means of delivering radiation to a ring of tissue outside the wall of a surgical cavity.

The 204 patent, which is a continuation-in-part of the 813 patent, describes an apparatus for brachytherapy and a method for using it for interstitial delivery of radiation to tissue proximate to the cavity formed by surgical removal of proliferative tissue. The apparatus includes a catheter body member having a proximal end and a distal end, an inner spatial volume proximate to the distal end of the catheter body member, an outer spatial volume defined by an expandable surface element proximate to the distal end of the body member and surrounding and concentric with the inner spatial volume. In the usual embodiment of the device, a radiation source is disposed in the inner spatial volume.

The 204 patent describes a number of embodiments that can be used with the device for delivery of radiation, including radioactive microspheres (Fig. 4), concentric non-spherical chambers (Fig. 5), a single solid radiation emitting material inside the catheter and an expandable cage defining the shape of the cavity (Fig. 6), a radioactive fluid filling the outer chamber (Fig. 7a), a radioactive fluid filling the inner chamber and the outer chamber filled with air or other radiation absorbing substance (Fig. 7b), and a single solid source in the catheter, surrounded by the outer chamber filled

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1 with radiation absorbing substance (Fig. 7c). Figure 7d shows examples of radiation profiles which
2 might be obtained by the embodiments shown in Fig. 7a – 7c where the depth of interest is shown as 2
3 cm from the surface of the outer volume. As can be seen, different embodiments can be used to vary
4 the ratio of the dose at the prescription depth, to the dose at the surface of the cavity.

5 **VII. THE MEANING OF THE DISPUTED CLAIM TERMS IN THE 813 AND 204**
6 **PATENTS TO ONE OF ORDINARY SKILL IN THE ART**

7 I have reviewed and relied upon the material listed in Section III above. Based upon these
8 materials, my own knowledge of the technical field to which the patented inventions relate, and my
9 familiarity with the level of ordinary skill in the art around the time that the 813 and 204 patents were
10 filed, I have formed opinions as to how one of ordinary skill in the art would have interpreted certain
11 claim terms at the time of the invention. My opinion of the meaning of each of these disputed terms is
12 set forth below. I have referenced the materials listed in Section III upon which I have relied for these
13 opinions. In situations where the disputed claim term is present in both patents 813 and 204, my
14 interpretation of the term is given only once. The list of disputed claim terms includes those identified
15 by either party in the case.

16
17 Radionuclide(s) – any radioactive isotope that is unstable and thereby decays into a different
18 isotope with the emission of radiation (Physics of Radiation Therapy”, p.12, see 813 2:50 – 2:55 for
19 examples).

20
21 Means for rendering uniform the radial dose profile –the radial dose profile is defined as the
22 absorbed dose to tissue as a function of distance from the center of the cavity along a particular
23 direction of interest. As described in the 813 patent, the points of interest in this profile would be from
24 the wall of the surgical cavity to a depth somewhat beyond that at which the prescription is defined.
25 The device provides a means for modifying the ratio of the dose at the depth of interest to the dose at
26 the surface of the cavity as desired for the particular clinical application, through manipulation of the
27 quantity and type of substances contained in the spatial volumes as shown in patent 813 Fig. 4 , also
28 1:59-67.

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1
2 Predetermined constant spacing – the spacing between the inner spatial volume and the wall of
3 the outer inflatable chamber can be made constant in all directions if the outer chamber is spherical
4 (Fig. 1 of 813), or constant along a radial direction if non-spherical (see Fig. 3 of 813 and 3:10-13),
5 whenever the outer chamber is inflated.

6
7 Outer closed inflatable chamber – this is a balloon or cage or inflatable chamber of any type
8 that can be made to be in contact with the surface of the surgical cavity when the catheter has been
9 inserted and the chamber is inflated (see 813 2:38-41).

10
11 Inner spatial volume – a region of space which is surrounded by the outer spatial volume
12 defined by a closed inflatable chamber. As shown in Fig. 1 of 813, it can be defined by the wall of an
13 inflatable chamber (see 2:34-36 of 813). As shown in Fig. 5 of 813 and 2:56-67 of patent 813, it can be
14 defined as the region of space containing a radiation source or an array of radiation sources. This is
15 also described in patent 204 2:56-60, 3:58-59, 4:4-7, 4:44-48 and 5:1-6.

16
17 The radioactive material – referred to in claim 8 in 813, this refers to any material containing
18 radionuclides, including microspheres, radioactive fluid or individual solid radioactive particle(s) that
19 can be enclosed in either of the spatial volumes. See patent 813 2:51-67 and 4:46-47.

20
21 Outer spatial volume – a region of space defined by an expandable surface element surrounding
22 an inner spatial volume (see patent 204 2:60-63, 4:4-5 and 8:22-23).

23
24 Brachytherapy – a method of treatment in which radioactive sources are used to deliver
25 radiation at a short distance by interstitial, intracavitary, or surface application (see “The Physics of
26 Radiation Therapy”, p. 418). As used in patent 204, 1:31 – 1:34, it is defined as radiation therapy
27 delivered by a spatially confined radioactive material inserted into the body at or near a tumor or other
28 proliferative tissue disease site

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1
2 Intraoperatively – this refers to the fact that the interstitial brachytherapy apparatus is placed
3 into the surgical resection cavity during the operation – i.e., after surgical removal of tumor, but prior
4 to closing the surgical site as indicated in patent 204 7:58 – 7:60.

5
6 Expandable surface element – an expandable or inflatable device such as a balloon or cage that
7 can be expanded or inflated in order to contact the inner surface of the surgical resection cavity (see
8 patent 204 2:61-63).

9
10 Radiation source – any device or material capable of generating radiation, such as radionuclides
11 or a high voltage electronic tube that can produce accelerated electrons which can be used directly to
12 irradiate cells or to produce x-rays through the interaction of these accelerated electrons with a target
13 (see patent 204 1:27-30, 1:47-50, 2:45-46 and 4:10-14).

14
15 Isodose profile – this would usually be a description of the dose received by points in tissue–
16 for example, a plot of dose vs. distance from the center of a source, or plurality of sources. As used in
17 5:12 – 5:41 in patent 204, it refers to 3-dimensional surfaces on which all points receive the same dose.

18
19 Surgical resection – surgical removal of tissue from the body (see patent 204 7:55-58).

20
21 Minimum prescribed dose – the minimum dose needed to destroy existing cancer cells in the
22 opinion of the physician (see line 52 in Fig.7d of patent 204).

23
24 Configuring the inner and outer spatial volumes to provide minimum prescribed absorbed dose
25 – as defined in claims 1, 19 and 32 of patent 204, where the radioactive material is disposed in the
26 inner spatial volume, the rate at which the dose falls off between the surface of the surgical cavity and
27 the depth at which the minimum dose is to be prescribed, can be controlled by modifying the quantity
28 and type of radiation absorbing material contained within the outer spatial volume. The safe delivery

1 of the minimum prescribed dose at the depth of interest requires that the tissue intervening between the
 2 surface of the cavity and the depth of interest receives a dose which is equal to, or greater than the
 3 prescribed dose but less than that which would necrose (i.e., lethally damage) healthy tissue. See
 4 patent 204 5:22-41 and 6:16 - 7:28.

5
 6 Minimum distance outward from the outer spatial volume expandable surface – the target tissue
 7 is defined as that tissue which is between the surface of the inflated outer spatial volume and a
 8 minimum distance outward from that surface, determined by the physician, to include the region in
 9 which tumor cells might reside (see patent 204 6:16-22 and Fig. 7d).

10
 11 Providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent
 12 necrosis in healthy tissue – by adjusting the distance between the radiation source and the surface of
 13 the outer spatial volume, or by adjusting the type of radiation absorbing material in the outer spatial
 14 volume, the ratio of the dose at the surface of the outer spatial volume to the dose at the depth of
 15 prescription, can be controlled (see patent 204 6:42 – 7:28 and Figs. 7a – 7d).

16
 17 Adapting the expandable surface to contact tissue surrounding the resection cavity to conform
 18 the tissue – the volume of the expandable surface can be adjusted by inflation until the surface of the
 19 expandable volume is in contact with the surface of the resection cavity at all points. In this state, the
 20 shape of the resection cavity conforms to the shape of the expandable surface (see patent 204 5:47-61).

21
 22 Desired shape of the expandable surface element – the desired shape of the expandable surface
 23 element is that shape which provides the predetermined constant spacing between the inner spatial
 24 volume and the conformed surface of the resection cavity (see patent 204 5:47-61).

25
 26 Delivering a prescribed absorbed dose – once the inflated expandable surface element is in
 27 contact with the surface of the surgical cavity, the dose at the prescription depth can be delivered once
 28 the radiation source is introduced into the catheter (see patent 204 5:66 – 6:28).

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1
2 Inner and outer volumes are configured to provide a minimum prescribed dose - see above.

3
4 Controlled dose – refers to controlling the ratio of doses at the depth of prescription to the dose
5 at the surface of the surgical cavity. See patent 204 6:42 – 7:28 and Figs. 7a-7d which show various
6 configurations to deliver minimum prescribed dose with variable doses to the surface of the surgical
7 cavity.

8
9 Reduce or prevent necrosis in healthy tissue proximate to the expandable surface – by
10 controlling the ratio of doses at the depth of prescription to the dose at the surface of the surgical cavity
11 through the use of different amounts and types of radiation absorbers in the inner and outer expandable
12 volumes, necrosis of healthy tissue in the vicinity of the surface of the surgical cavity can be prevented
13 or reduced. See patent 204 6:42 – 7:28 and Figs. 7a-7d which show various configurations to deliver
14 minimum prescribed dose while reducing or preventing necrosis in proximate healthy tissue.

15
16 Predetermined spacing – the spacing between the inner and outer spatial volumes can be set to
17 a predetermined and constant value by modifying the level of inflation or expansion of one or both
18 volumes (see patent 204 5:22-32).

19
20 Interstitial – pertaining to or situated in the interspaces of a tissue. These interspaces are not
21 naturally occurring. See patent 204 1:31-34 and December 20, 2000 amendment at pages 11-15 and
22 “The Physics of Radiation Therapy” at pages 457-458.

23
24 A plurality of radioactive solid particles placed at pre-determined locations within the inner
25 spatial volume to provide a desired composite radiation profile – as shown in Figure 5 of patent 813,
26 and as described in 2:64– 3:9, a plurality of radioactive particles which can be positioned in such a way
27 as to generate a desired dose profile.

28
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Interstitial brachytherapy – short distance radiation therapy applied directly into the interspaces of tissue in a cavity that is not naturally occurring (see “Physics of Radiation Therapy” pages 418 and 457-458).

Three-dimensional isodose profile – a three dimensional surface on which the radiation dose is the same at all points (see patent 204 5:16-19).

Solid radiation source – a radiation source that has a fixed shape and volume and is not deformable (see patent 204 4:44-48 and 4:54-56).

The prescribed absorbed dose is delivered to the target tissue in substantially three dimensions – as described in claim 18 of patent 204, this refers to the fact that, once the outer chamber is expanded, the tissue surrounding the chamber conforms to the shape of the chamber, thereby assuring that all points in tissue that are a fixed distance from the wall of the surgical cavity will receive the identical dose.

Extrinsic Evidence

The Physics of Radiation Therapy by Faiz Khan, p. 12 (radioactivity and radionuclides), p. 418 (brachytherapy), p. 457-458 (interstitial brachytherapy)

VIII. DEMONSTRATIVES

I understand that I might be requested to provide a tutorial regarding the technology of the 813 and 204 patents. I would expect to deliver this information using a combination of Powerpoint slides and photocopied material that I have used previously in the teaching of the Physics of Radiation Oncology to professionals and students.

IX. OTHER CASES IN WHICH I HAVE TESTIFIED DURING THE PAST FOUR YEARS

I have provided testimony as an expert at a deposition in the case of *Maggiani vs. University of Southern California* on February 20, 2006.

1 **X. COMPENSATION**

2 I am being compensated for my work on this matter at a rate of \$500 per hour. My
3 compensation does not depend on the outcome of this case.

4 * * *

5 I declare under penalty of perjury that the foregoing statements are true and correct.

6 Dated: October 12, 2006

San Francisco, California

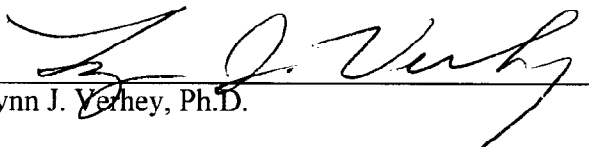
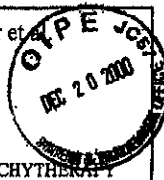
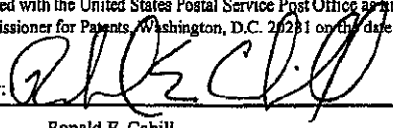
7
8 
9 _____
Lynn J. Verhey, Ph.D.

Exhibit 9

#7/A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Rance A. Winkler et al.		Group Art Unit: 3736
Application No:	09/293,524		Examiner: J. Lacyk
Filing Date:	April 15, 1999		
Entitled:	INTERSTITIAL BRACHYTHERAPY APPARATUS AND METHOD FOR TREATMENT OF PROLIFERATIVE TISSUE DISEASES		
Atty. Docket No:	101360-15 (ONE-008)		

<u>Certificate of Mailing (37 C.F.R. 1.8(a))</u>	
I hereby certify that this correspondence is being deposited with the United States Postal Service Post Office as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on the date set forth below.	
December 20, 2000	By: 
Date of Signature and Mail Deposit	Ronald E. Cahill Reg. No: 38,403

AMENDMENT AND RESPONSE

Assistant Commissioner for Patents
Washington, DC 20231

Dear Sir:

In response to the Office Action dated June 20, 2000, please amend the above-referenced patent application as follows:

12/27/2000 MAILED 00000057 09293524

02 FC:202	<u>In the claims</u>	120.00 OP
03 FC:203		18.00 OP

Please amend the claims as follows:

A

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Group Art Unit: 3736
Examiner: J. Lacyk
Atty Docket No: 101360-15 (ONE-008)

CLAIMS

1. (Amended) An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:

- (a) a catheter body member having a proximal end and distal end;
- (b) an inner spatial volume disposed proximate to the distal end of the catheter body member;
- (c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
- (d) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

A1
2. (Amended) The apparatus of claim 1, wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue [that may include cancer cells], the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

A2
4. (Amended) The apparatus of claim 3, wherein the expandable surface element is adapted to contact [contacts] tissue surrounding a resected cavity and adapted to conform [conforms] the tissue to the desired shape of the expandable surface element.

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Please cancel claims 5 and 6.

~~17~~ ^{A3} (Amended) The apparatus of claim ~~13~~, wherein [the] a burst strength of the distensible chamber defining the outer spatial volume is greater than [the] a burst strength of the chamber defining the inner spatial volume.

- ^{A4} ~~19~~ ²¹ (Amended) A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:
- (a) surgically creating access to the proliferating tissue in a patient;
 - (b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;
 - (c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:
 - (i) a catheter body member having a proximal end and distal end;
 - (ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;
 - (iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
 - (iv) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element;
 - (d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity until a prescribed absorbed dose has been delivered to tissue surrounding the apparatus; and
 - (e) removing the interstitial brachytherapy apparatus.

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²⁰
22. (Amended) The method of claim ¹⁹21, further including placing [wherein] the radioactive source [is placed] into the interstitial brachytherapy apparatus after the step of placing [placement of] the apparatus into the tumor resection cavity.

²¹
23. (Amended) The method of claim ¹⁹21, further including removing [wherein] the radioactive source [is removed] from the interstitial brachytherapy apparatus before the step of removing [removal of] the apparatus.

²²
24. (Amended) The method of claim ¹⁹21, wherein the proliferating tissue is [resected from] a patient's brain.

AH ²³
25. (Amended) The method of claim ¹⁹21, wherein the proliferating tissue is [resected from] a patient's breast.

²⁴
26. (Amended) The method of claim ¹⁹21, further including configuring [wherein] the inner and outer spatial volumes [are configured] to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue [that may include cancer cells], the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

²⁵
27. (Amended) The method of claim ²⁴26, further including providing [wherein] a predetermined spacing [is provided] between said inner spatial volume and the expandable surface element.

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26
28. (Amended) The method of claim 25, wherein the expandable surface element is adapted to contact [contacts] tissue surrounding a resected cavity and adapted to conform [conforms] the tissue to the desired shape of the expandable surface element.

Please cancel claims 29 and 30.

Please add the following new claims:

24
31. The method of claim 26, wherein the step of configuring the inner and outer spatial volumes includes expanding the inner and outer spatial volumes.

32
36. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

- A5
- (a) surgically creating access to the proliferating tissue in a patient;
 - (b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;
 - (c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:
 - (i) a catheter body member having a proximal end and distal end;
 - (ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;
 - (iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
 - (iv) a radiation source disposed in the inner spatial volume;

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(d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity;

(e) configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface; and

(f) removing the interstitial brachytherapy apparatus.

³³
37. The method of claim ³²36, wherein the step of configuring the inner and outer spatial volumes includes expanding the inner and outer spatial volumes.

³⁴
AS 38. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

- (a) surgically creating access to the proliferating tissue in a patient;
- (b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;
- (c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:
 - (i) a catheter body member having a proximal end and distal end;
 - (ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;
 - (iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

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- (iv) a radiation source disposed in the inner spatial volume;
- (d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity;
- (e) adapting the expandable surface element to contact tissue surrounding the resection cavity to conform the tissue to the desired shape of the expandable surface element;
- (f) delivering a prescribed absorbed dose to tissue surrounding the apparatus; and
- (g) removing the interstitial brachytherapy apparatus.

³⁵
39. The method of claim ³⁴36, wherein the step of adapting the expandable surface element includes expanding the outer surface volume.

³⁶
AS 40. An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:

- (a) a catheter body member having a proximal end and distal end;
- (b) an inner spatial volume disposed proximate to the distal end of the catheter body member;
- (c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

- (d) a radiation source disposed in the inner spatial volume;

wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

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REMARKS

The above-identified patent application has been amended and reconsideration is respectfully requested. In response to the Examiner's rejections, Applicant hereby amends claims 1, 2, 4, 14, and 21-28. Claims 5, 6, 29, and 30 are canceled. Claims 35-40 are added. Claims 1 and 21, as amended, now recite that the interstitial brachytherapy apparatus comprises a radiation source disposed in the inner spatial volume that generates a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element. Accordingly, claims 5, 6, 29, and 30 are canceled. New independent claim 36 incorporates all of the limitations of claims 21 and 26, while new independent claim 38 incorporates all of the limitations of claims 21 and 28. Also, new independent claim 40 incorporates all of the limitations of claims 1 and 2. New dependent claims 35 and 37 recite that the step of configuring the inner and outer spatial volumes includes expanding the inner and outer volumes, while new dependent claim 39 recites that the step of adapting the expandable surface element includes expanding the outer surface volume. Support for these limitations can be found on page 7, line 27 to page 8, line 15. Accordingly, no new matter is added by these amendments.

Response to the Indefiniteness Rejections

Claims 2, 4, 5, 14, and 22-29 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for unclear language and for lacking antecedent basis for certain limitations.

The Examiner rejects claims 2 and 26 for use of the phrase "may include" in line 3, which is alleged to render the claims indefinite. Accordingly, the phrase "that may include cancer cells" has been deleted from claims 2 and 26. In addition, claims 2 and 26 are amended to recite a "minimum *prescribed* absorbed dose" to provide proper antecedent basis for dependent claims.

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Claims 4 and 28 are rejected for containing language which appears to claim a positive connection to the body. As helpfully suggested by the examiner, Applicant amends claims 4 and 28 to recite that the expandable surface element is "adapted to contact tissue surrounding a resected cavity and adapted to conform the tissue to the desired shape of the expandable surface element."

The Examiner rejects claims 5 and 29 for failing to include structure to support how the apparatus "creates absorbed isodose profiles." Applicant respectfully traverses the Examiner's indefiniteness rejections, for the following reasons. Amended claims 1 and 21 now recite that the radiation source disposed in the inner spatial volume generates a three-dimensional isodose profile. Inasmuch as claims 5 and 29 depend upon claims 1 and 21, respectively, the limitation that the radiation source generates the isodose profile should provide the sufficient structural support sought by the Examiner. Thus, Applicant respectfully argues that the structural support required for the limitations in claims 5 and 29 are present. Examiner is asked to kindly reconsider his rejections in view of amended claims 1 and 21.

Claim 14 was rejected for failing to provide antecedent basis for the limitation "the burst strength". In response, claim 14 is amended to provide antecedent basis for such limitation.

The Examiner rejects claims 22-29 for failing to recite method limitations in the active state. Accordingly, claims 22, 23, and 26-28 are amended to place such method steps in the active tense. Claims 24 and 25 further define structural limitations and therefore do not need to be placed in the active tense. However, claims 24 and 25 are amended to clarify that a structural limitation is being recited, not a method limitation. And claim 29, as written, is already in the active tense.

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Applicant believes that such amendments to claims 2, 4, 5, 14, and 22-29 satisfy the requirements of the examiner, and respectfully request that the indefiniteness rejections over those claims be withdrawn.

Response to the Non-Statutory Double Patenting Rejection

Claims 1-14 and 18-34 stand rejected under the judicially created doctrine of double patenting over claims 1-13 of U.S. Patent No. 5,913,813. Accordingly, provided herewith is a timely filed terminal disclaimer in compliance with 37 C.F.R. 1.321(c) to overcome the Examiner's rejection based on a non-statutory double patenting ground, since the patent is commonly owned with this application. Applicant respectfully requests that the Examiner indicate receipt and acceptance of the terminal disclaimer, and withdrawal of the non-statutory double patenting rejection over claims 1-14 and 18-34 of the present application in his next correspondence.

Response to the Anticipation Rejection

Claim 1 stands rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Ishiwara et al., U.S. Patent No. 5,106,360 (hereinafter "Ishiwara"). Claim 1 also stands rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Weinberger, U.S. Patent No. 5,924,973. Based on the amendments and the following remarks, Applicant respectfully requests reconsideration and withdrawal of the rejections under both Ishiwara and Weinberger.

Applicant's invention relates to an interstitial brachytherapy apparatus for providing radiation treatment to proliferative tissue in a living patient. The apparatus includes a catheter body member, an inner spatial volume disposed at a proximal end of the catheter body member, an outer spatial volume defined by an expandable surface element which surrounds the inner spatial volume, and a radiation source disposed in the inner spatial volume. The radiation source

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generates a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

Turning to the cited prior art, the Ishiwara device comprises a thermotherapeutic apparatus having a catheter body member, an inner lumen surrounded by an outer lumen, and a radiation source contained within the inner lumen. As disclosed in col. 4, lines 19-23, Ishiwara's apparatus is inserted into a body cavity. See, e.g., Figure 4. Hence, the apparatus does not provide *interstitial* radiation treatment, as Applicant's invention requires, but rather intercavitary radiation treatment. Such a distinction is significant when considering the isodose profiles generated by the two devices. In the apparatus of Ishiwara, the isodose profiles do not take the shape of the outer lumen. Rather, the radiation source generates absorbed isodoses along the sides of the outer lumen, and not at the ends. This is because Ishiwara is concerned with tumor growth along a cavity, and therefore would not require radiation at the ends of the lumen.

Applicant respectfully reminds the Examiner that in a related parent application, 08/900,021, wherein Ishiwara was also cited, Applicant had argued that:

In the Ishiwara et al. '360 patent relied upon for anticipation, the outer chamber defined by the radiation transparent wall 12 cannot provide a uniform radiation profile. The outer balloon 12 in the Ishiwara et al. patent functions only to stabilize the device within and hold a thermal mass (liquid) against surrounding tissue so that it can be warmed or cooled by thermal conduction. There is no teaching or suggestion in the patent of how to provide a uniform radial absorbed dose profile of emissions emanating from the liquid radiation source 38. Moreover, given the banana shape of the Ishiwara device, the profile will be much different proximate the distal and proximal ends of the balloon 12 than in its central tissue contacting region. Thus, it cannot be said that applicants' invention, as claimed, is taught by or inherent in the Ishiwara '360 device.

In that instance, Applicant's arguments with respect to Ishiwara were deemed persuasive by the Examiner in the parent application. Applicant believes that much of the arguments

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proposed to the Examiner in the parent application are applicable to the present invention. Examiner is asked to kindly refer to Figure 5 of Ishiwara, which shows the banana shape of the device. As illustrated, the outer surface element is not substantially the same shape as the inner spatial volume. Therefore, the radiation source disposed in the inner spatial volume of Ishiwara would not generate a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

Similarly, Weinberger discloses in Figure 17 an intercavitary radiotherapy device for insertion within a patient's lumen. See col. 4, lines 61-65 and col. 4, lines 22-28. Like Ishiwara, Weinberger's apparatus does not provide *interstitial* radiation treatment, as Applicant's invention requires, but instead *intraluminal* radiation treatment. Whereas Applicant's device treats disease that is embedded in tissue (e.g., breast cancer), Ishiwara and Weinberger treat disease in a luminal cavity. For this reason, in Ishiwara and Weinberger, the catheters and expandable balloons are very different than those of Applicant's invention. Ishiwara and Weinberger require a catheter that can work with a guidewire for insertion into a lumen, while Applicant's catheter does not need to work with a guidewire, since Applicant's apparatus is inserted into tissue rather than a hollow lumen. Effectively, this results in Applicant's catheter being differently sized and shaped relative to the catheters of Ishiwara and Weinberger. Applicant's catheter allows the inner volume to closely match the shape of the outer expandable element, hence allowing the radiation source inside the inner volume to generate a three-dimensional isodose profile that is substantially similar in shape to the outer expandable element.

In contrast, due to the configuration of the catheters, the inner volumes of Ishiwara and Weinberger are not substantially similar in shape to their outer expandable elements. The distinction is significant when considering the three-dimensional isodose profiles generated by the two devices. Ishiwara and Weinberger do not provide an apparatus that can produce isodose

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profiles that are substantially similar in shape to the outer lumen. For example, referring to Figure 17 of Weinberger, a large diameter catheter 200 runs through the double balloons 202, 204 of the device. It is clear from this illustration that, given the large size of the Weinberger catheter and the fact that the ends of the balloons do not generate absorbed isodose profiles, the device does not generate a three-dimensional isodose profile that is substantially similar in shape to the outer expandable element.

As amended, independent claims 1 and 21 require an interstitial brachytherapy apparatus having a radiation source disposed in the inner spatial volume that generates a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element. These recitations are neither taught nor suggested by Ishiwara or Weinberger. As discussed *supra*, both Ishiwara and Weinberger disclose an intercavitary radiation device that operates differently and generates a different radiative effect than Applicant's interstitial radiotherapy device. Because Ishiwara and Weinberger fail to disclose each and every limitation of the claimed invention, the Examiner is kindly asked to reconsider his rejections under Ishiwara and Weinberger, and withdraw these rejections in his next office action.

Finally, since Ishiwara and Weinberger pertain to intraluminal radiation treatment devices rather than interstitial radiation treatment devices, Applicant urges that Ishiwara and Weinberger fail to disclose or teach an expandable surface element that is adapted to contact tissue surrounding a resected cavity and conform the tissue to the desired shape of the expandable surface element, as is recited in claim 4. In addition, because Ishiwara and Weinberger do not provide an apparatus that can produce isodose profiles that are substantially similar in shape to the expandable surface element, particularly in three dimensions, Applicant urges that claims 5 and 6 are not rendered to be anticipated or obvious by Ishiwara and Weinberger. Therefore, the

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Examiner is kindly asked to acknowledge the allowability of these claims in his next office action.

Claim 1 stands rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Bradshaw et al., U.S. Patent No. 5,662,580 (hereinafter "Bradshaw"). Based on the amendments and the following remarks, applicant respectfully requests reconsideration and withdrawal of the rejection under Bradshaw.

As discussed *supra*, Applicant's invention relates to an interstitial brachytherapy apparatus for providing radiation treatment to proliferative tissue in a living patient. The apparatus includes a catheter body member, an inner spatial volume disposed at a proximate end of the catheter body member, an outer spatial volume defined by an expandable surface element which surrounds the inner spatial volume, and a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

In contrast to Applicant's invention, Bradshaw discloses an intercavitary radiotherapy device for insertion within a patient's blood vessel, rather than an interstitial radiotherapy apparatus. See col. 5, lines 11-14. Bradshaw's device thus does not create absorbed isodose profiles shaped substantially similar to the outer lumen of the device. The Examiner is kindly referred to the discussion *supra* for reasons why an intercavitary radiotherapy device functions in a different manner than an interstitial radiotherapy device, and hence produces a different isodose profile. Furthermore, Bradshaw discloses in col. 5, lines 15-30 that the *outer* lumen of the balloon catheter is filled with isotopes, rather than the inner lumen, as required in claim 1. Bradshaw therefore teaches the exact opposite of Applicant's claimed invention. Rather than have the isotopes radiate out from an internal lumen, the isotopes in Bradshaw are placed within

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the outer lumen contacting the vessel wall. For this reason, Applicant respectfully argues that the claimed invention is neither anticipated by or rendered obvious by Bradshaw. The Examiner is kindly asked to reconsider his rejection under Bradshaw and withdraw this rejection in his next office action.

Finally, since Bradshaw relates to an intraluminal radiation treatment device rather than an interstitial radiation treatment device, Applicant urges that Bradshaw fails to disclose or teach an expandable surface element that is adapted to contact tissue surrounding a resected cavity and conform the tissue to the desired shape of the expandable surface element, as is recited in claim 4. In addition, because Bradshaw does not provide an apparatus that can produce isodose profiles that are substantially similar in shape to the expandable surface element, especially in three dimensions, Applicant urges that claims 5 and 6 are not rendered to be anticipated or obvious by Bradshaw. Therefore, the Examiner is kindly asked to acknowledge the allowability of these claims in his next office action.

Claims 1 and 21-24 stand rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Williams, U.S. Patent No. 5,429,582. Based on the amendments and the following remarks, applicant respectfully requests reconsideration and withdrawal of the rejection under Williams.

Amended claims 1 and 21 now require that the interstitial brachytherapy apparatus comprise a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element. As seen in Figure 7 of Williams, outer lumen 28B is not evenly spaced apart from inner lumen 28A that contains the radiation source. In this system, where the radiation source is provided as a liquid within the inner balloon, the shape of the three-dimensional isodose profile will correspond to the shape of the inner balloon. For this reason, Williams does not provide an

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apparatus that can generate a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element, as is recited in the claims. That is, because the balloons are not equally spaced apart, Williams' apparatus cannot create an isodose profile that has substantially the same shape as the outer element. Hence, Williams fails to disclose each and every limitation of the claimed invention. Based on Applicant's arguments, the Examiner is kindly asked to reconsider his rejection under Williams and withdraw this rejection in his next office action.

Finally, since compression of the brain tissue surrounding the outer balloon 28B (see Figure 7) might prove detrimental to the health of the patient, Applicant urges that Williams fails to disclose or teach an expandable surface element that is adapted to contact tissue surrounding a resected cavity and conform the tissue to the desired shape of the expandable surface element, as is recited in claims 4 and 28. In addition, because William does not provide an apparatus that can produce isodose profiles that are substantially similar in shape to the expandable surface element, particularly in three dimensions, Applicant urges that claims 5, 6, 29, and 30 are not rendered to be anticipated or obvious by Williams. Therefore, the Examiner is kindly asked to acknowledge the allowability of these claims in his next office action.

Response to the Obviousness Rejections

Claim 25 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Williams.

On page 4 of the Office Action, the examiner asserts that:

Although Williams does not specifically disclose using the device to treat the breast, a modification of Williams to do so would have been obvious to one of ordinary skill in the art at the time the invention was made in that one skilled in the art would readily know that the device could be used in any part of the body to treat tissue surrounding a cavity left by surgical removal of a tumor.

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Applicant respectfully disagrees with the examiner's assertions and kindly refers the examiner to the discussion *supra* for reasons why Williams fails to satisfy the limitations of claim 21, as amended. Inasmuch as claim 25 depends upon claim 21, which claim was previously argued by applicant to be unanticipated by Williams, discussion of the rejection of claim 25 over the same prior art is rendered unnecessary. The Examiner is asked to kindly reconsider his rejection of claim 25 over Williams, and withdraw this rejection in his next office action.

Additionally, claims 15-18 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Weinberger or Bradshaw in view of Clerc et al., U.S. Patent No. 6,059,812 (hereinafter "Clerc"). On pages 4 and 5 of the Office Action, the examiner asserts that:

Bradshaw et al and Weinberger disclose the claimed device except for the use of an expandable cage instead of a balloon. Clerc et al. discloses a self-expanding "cage" (12) that is used to help deliver radioactive therapy. Clerc et al. discloses the support having a shape memory such that it is self opening. Further to use any known shape memory material such as nitinol would have been obvious since nitinol is well known and conventionally used with radioactive therapy devices. Therefore a modification of Bradshaw et al or Weinberger such that a "cage" or support is used instead of a balloon would have been obvious.

For several reasons, applicant respectfully disagrees with the examiner's assertion that these combinations would satisfy the limitations of the claimed invention. In particular, Applicant respectfully disagrees with the examiner's assertions that Bradshaw and Weinberger disclose the claimed device except for the use of an expandable cage instead of a balloon. The Examiner is kindly referred to the discussion *supra* for reasons why both Weinberger and Bradshaw fail to clearly anticipate the claimed invention. Thus, inasmuch as claims 15-18 depend upon claim 1, which claim was previously argued by applicant to be unanticipated by Weinberger and Bradshaw, discussion of the rejection of claims 15-18 over the same prior art is rendered unnecessary.

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Because the admitted deficiencies of Weinberger and Bradshaw are not overcome by their combination with Clerc, applicant respectfully requests that the examiner withdraw the obviousness rejections under Weinberger and Bradshaw in view of Clerc in his next office action.

Finally, in reviewing the prior art cited by the examiner, Applicant urges that none of the references either anticipate or render obvious the

Newly Added Claims are Not Anticipated by the Prior Art

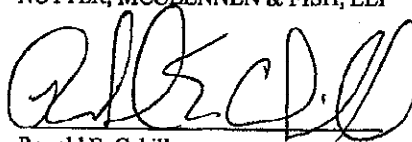
Newly added claim 35 depends upon claim 26, which claim was not rejected over prior art, and should therefore be allowable. New claim 36 includes all the limitations of claim 21 and claim 26, which claim was not rejected under prior art. Similarly, newly added claim 38 includes all the limitations of claims 21 and claim 28, which claim was not rejected under prior art. New claim 40 includes all the limitations of claims 1 and 2, which claim was not rejected over prior art. New claims 37 and 39 depend from new claims 36 and 38, respectively. Therefore, Applicant believes that new claims 35-40 are allowable over the cited prior art.

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For all of the foregoing reasons, Applicants request that the Examiner reconsider the rejection of claims 1-34 and allow claims 1-34, along with newly added claims 35-40 to issue. If the Examiner believes that an interview would facilitate the resolution of any outstanding issues, the Examiner is kindly requested to contact the undersigned.

Respectfully submitted,

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Exhibit 10



US005429582A

United States Patent [19]

Williams

[11] Patent Number: 5,429,582

[45] Date of Patent: Jul. 4, 1995

[54] TUMOR TREATMENT

[76] Inventor: Jeffery A. Williams, 608 NE. 18th St., Oklahoma City, Okla. 73105

[21] Appl. No.: 715,923

[22] Filed: Jun. 14, 1991

[51] Int. Cl.⁶ A61N 5/02

[52] U.S. Cl. 600/2; 607/3

[58] Field of Search 600/1-4;
604/20, 19; 607/1-3, 88, 96, 99, 100, 107, 103,
105, 113, 114

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Primary Examiner—Angela D. Sykes

Assistant Examiner—John P. Lacyk

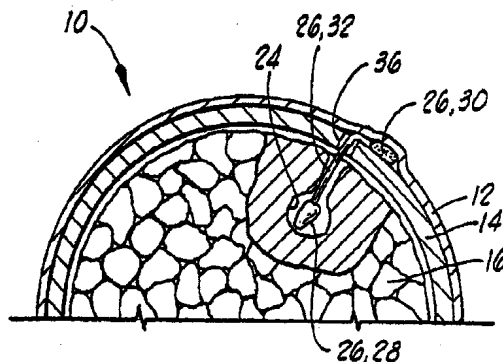
Attorney, Agent, or Firm—Dougherty, Hessin, Beavers & Gilbert

[57]

ABSTRACT

A completely implantable apparatus is provided for treatment of tissue surrounding a cavity left by surgical removal of a brain tumor. The apparatus includes an inflatable balloon constructed for placement in the cavity. A subcutaneously implantable treatment fluid receptacle is provided for receiving a transdermal injection of a treatment fluid. A catheter connects the receptacle to the inflatable balloon. Various embodiments provide for simultaneous application of heat therapy and/or radiation therapy and/or chemotherapy to the remaining tissue surrounding the cavity from which the tumor was removed.

38 Claims, 4 Drawing Sheets



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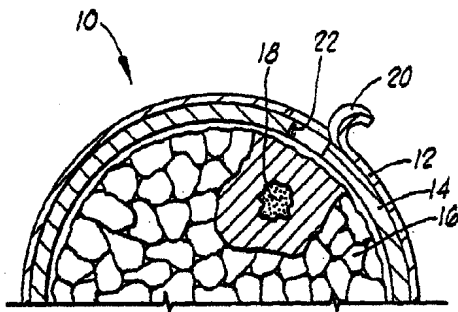


FIG. 1

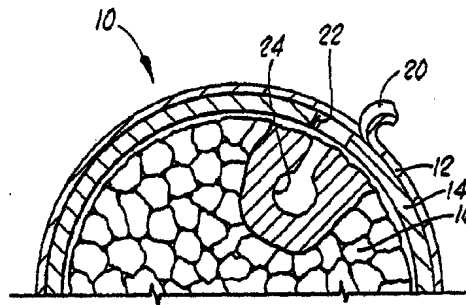


FIG. 2

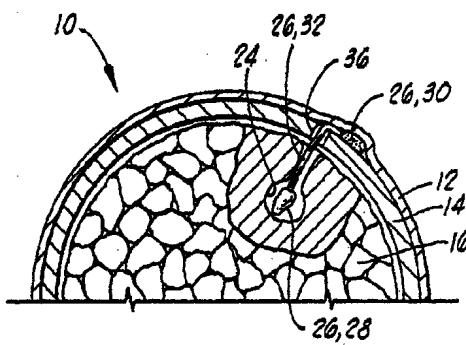


FIG. 3

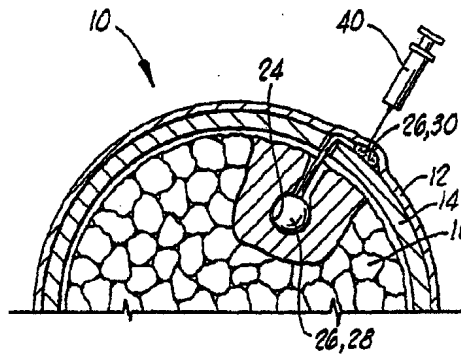


FIG. 4

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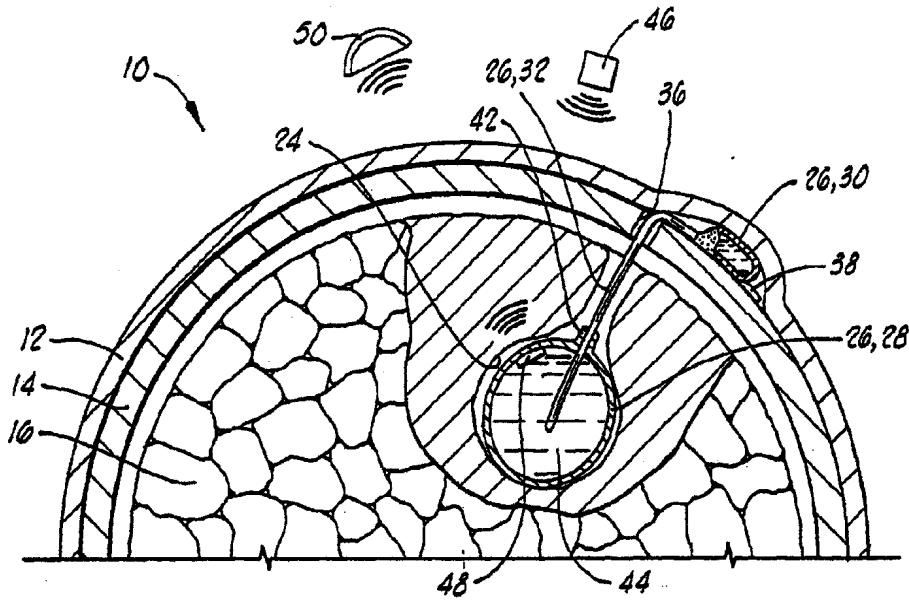


FIG. 5

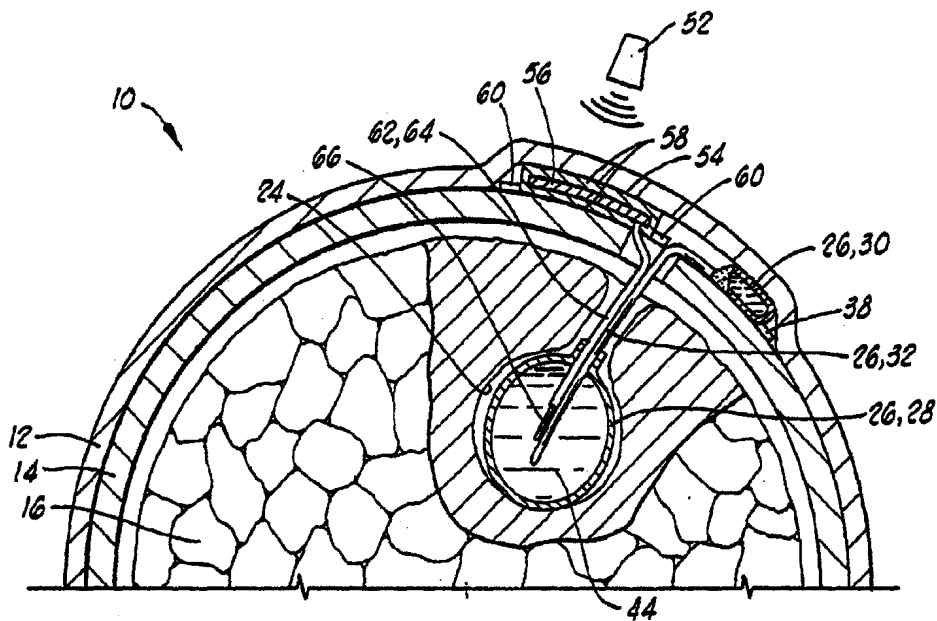
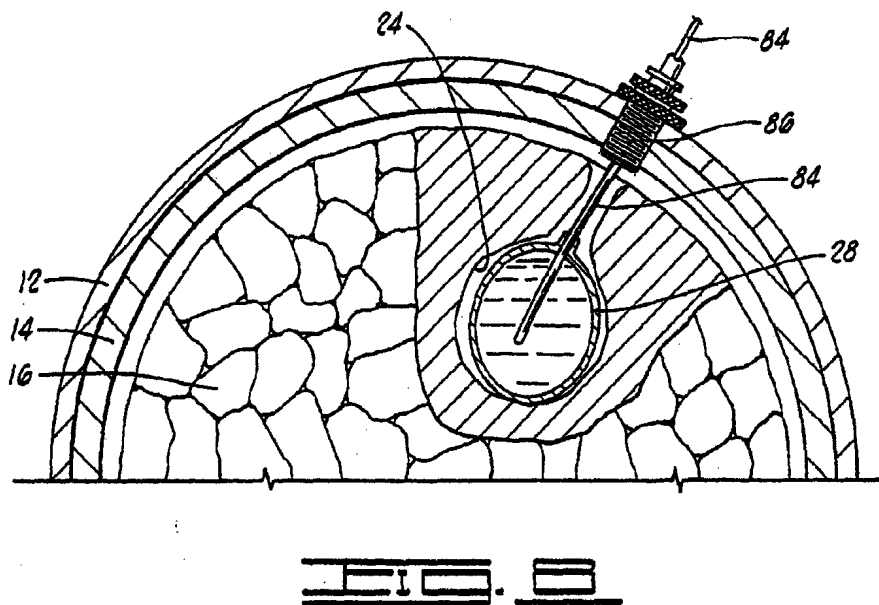
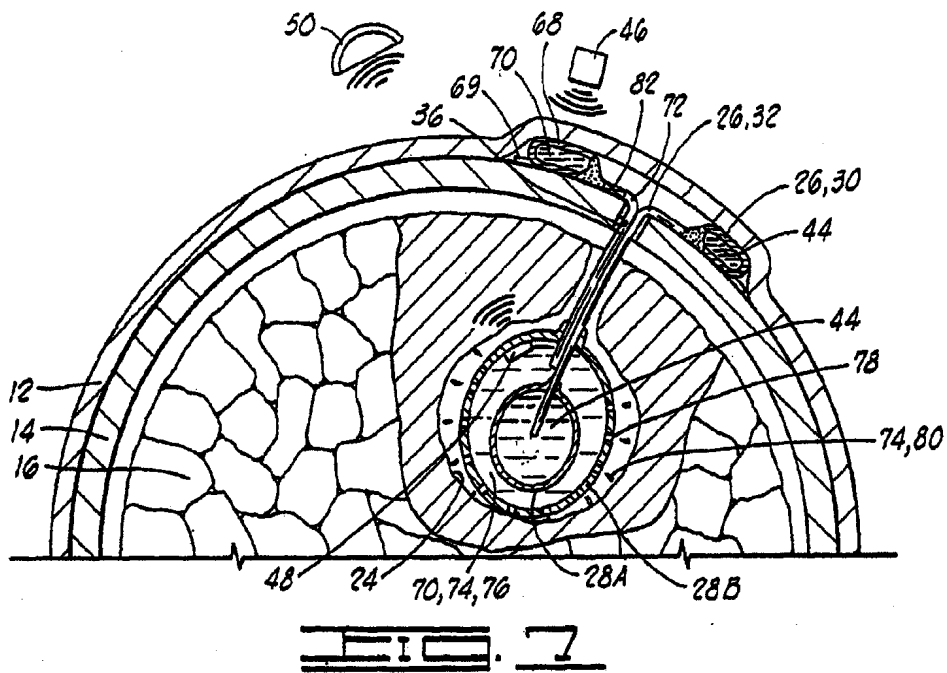


FIG. 6

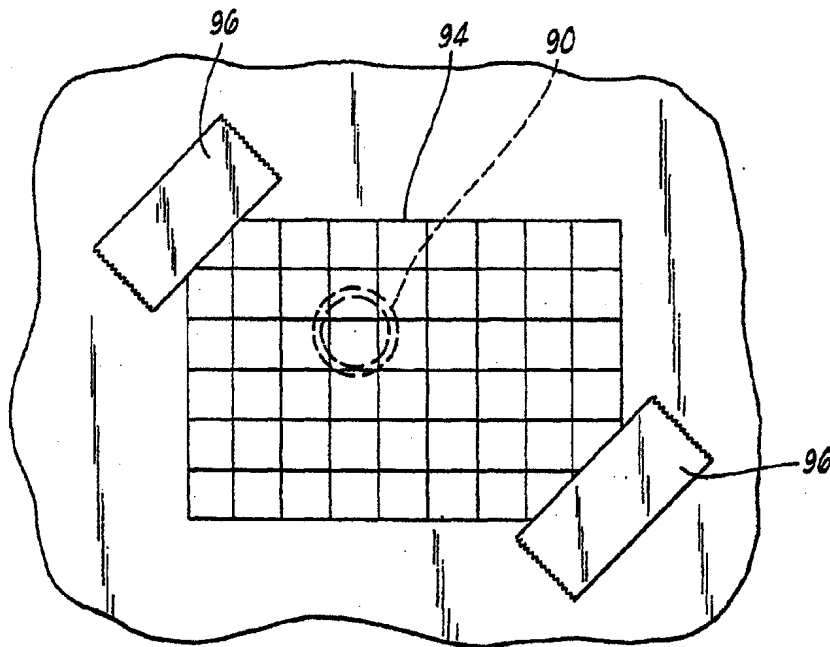
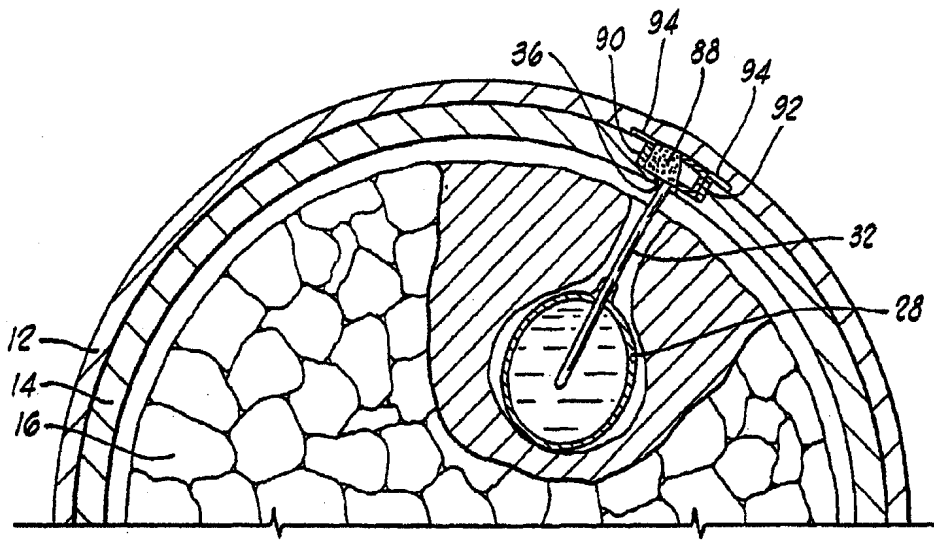


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TUMOR TREATMENT

BACKGROUND OF THE INVENTION

1. Field Of The Invention

The present invention relates to apparatus and methods for the treatment of tumors in a living body, and more particularly, but not by way of limitation, to apparatus and methods for treatment of brain tumors in a human.

2. Description of the Prior Art

Conventional techniques of post-operative treatment of residual tumor following only gross removal of tumor include sequential, but not simultaneous administration of radiation, chemotherapy, and/or heat. Simultaneous administration of these modalities to the residual tumor is advantageous but impossible utilizing currently available techniques.

Further, no currently available intraoperative therapeutic procedure utilizes the cavity formerly occupied by the bulk of the tumor for placement of an inflatable device for subsequent tumor therapy, whether combined (radiation and/or chemotherapy and/or hyperthermia together) or single modality (one of the above alone), or whether simultaneous or sequential in application.

The current practice of brachytherapy (implantation of radioactive sources in the tumor and surrounding tissue) requires simultaneous placement of numerous separate catheters. Placement of catheters for afterloading must currently incorporate pre-operative placement of a stereotactic frame for localization, a procedure which is expensive, cumbersome, and time-consuming. In frame placement, a large heavy frame is attached to the skull of the awake patient utilizing transdermal metal screws and local anesthetic, often not a smooth or desirable procedure. Once the frame is placed, a CT scan and extensive calculations are required before the patient is transported to the operating room, with the frame on his or her head, for the actual catheter placements. This second transport is cumbersome.

Once in the operating room, numerous separate holes (usually up to 24) are manually drilled in the patient's scalp and skull. Then existing catheters are placed to the appropriate depth and sewn into place. These catheters are subsequently afterloaded with solid isotopic pellets for a prescribed time. The pellets are removed and, if hyperthermia is desired, separate metal antennae are loaded into the existing catheters for subsequent heating and thermometry. Although reasonably proximal in time, these sequential loadings reduce the efficacy of combined treatment, which should be simultaneous for highest tumor kill. During treatment, the catheters are externally exposed with attendant risk of infection.

Following delivery of the prescribed radiation and heat, the catheters are removed. Any subsequent treatment, as for example following tumor recurrence, would require repeating the entire sequence described above.

SUMMARY OF THE INVENTION

For these reasons, it would be desirable to provide methods and apparatus for initial intra-operative placement of a completely implantable device for subsequent simultaneous hyperthermia and/or radiation and/or chemotherapy treatment for brain tumors or tumors in

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other sites. Just such a system is provided by the present invention.

An implantable apparatus is provided for treatment of tissue surrounding a cavity left by surgical removal of a tumor from a living patient. The apparatus includes an inflatable balloon constructed for placement in the cavity. A treatment fluid receptacle means is provided for receiving a transdermal injection of a treatment fluid. A catheter means is connected between the receptacle means and the balloon for carrying the treatment fluid from the receptacle means to the inflatable balloon.

The treatment fluid can be a radioactive treatment fluid or a chemotherapy fluid, or in one embodiment a double-wall balloon is provided so that both a radioactive treatment fluid and a chemotherapy fluid can be simultaneously applied.

Various means are provided for heating the treatment fluids thus also providing the alternative of simultaneous heat therapy.

Monitoring means are provided for monitoring the temperature of the treatment fluid in the balloon.

The invention provides a significant advantage in that it provides a means for simultaneous administration of radiation therapy and/or chemotherapy and/or heat therapy.

Another advantage is that a treatment device is intraoperatively placed in the cavity formerly occupied by the bulk of the tumor thus providing a means for subsequent treatment of residual tumor without further surgical incisions.

Another advantage is that the distensible balloon takes advantage of the inherent natural compliance of a fluid to conform to the outline of the cavity to be treated, thus allowing close approximation of the treatment device to the treated residual tumor.

The present invention also takes advantage of the greater variety of desirable physical or superior cost properties inherent in readily available liquid isotopes. These liquid isotopes are cheaper and possess higher specific activities (millicuries per gram) when compared to their conventional, solid counterparts. This is a highly desirable characteristic which allows a higher concentration of radioactivity to be administered, thus resulting in higher tumor cell kill.

Another advantage of the present invention is that it allows homogeneous mixing of disparate treatment agents for the uniform administration of hyperthermia and brachytherapy simultaneously to a human tumor surrounding a post-operative cavity.

Numerous other objects, features and advantages of the present invention will be readily apparent to those skilled in the art upon a reading of the following disclosure when taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGS. 1-4 comprise a sequential series of schematic elevation sectioned drawings through the coronal portion of the head of a human being. In FIG. 1 the scalp has been laid back and one or more burr holes are placed in the skull allowing creation of a circular bone flap which when temporarily removed allows gross resection of the tumor. In FIG. 2 the major portion of a brain tumor has been operatively removed. In FIG. 3 intra-operative placement of the implantable apparatus of the present invention has been accomplished and the incision has been closed. In FIG. 4 a hypodermic needle is used to transdermally place a treatment fluid in the

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apparatus to inflate the distensible catheter in place within the cavity formed by removal of the tumor.

FIG. 5 is an enlarged view similar to FIG. 4 illustrating further details of the apparatus including means for heating and means for monitoring the temperature of the fluid in the balloon.

FIG. 6 is a view similar to FIG. 5 illustrating alternative means for heating.

FIG. 7 is a view similar to FIG. 5 illustrating an alternative embodiment of the invention having a double-wall balloon to allow chemotherapy treatments.

FIG. 8 is a view similar to FIG. 5 of another alternative embodiment which is not completely implantable, and which has the catheter extending through a bolt means placed in the skull.

FIG. 9 is a view similar to FIG. 5 of another alternative embodiment having a treatment fluid receptacle countersunk within the skull so as to avoid deformation of the overlying scalp. The implantable receptacle includes a metallic ring which is visible to X-rays.

FIG. 10 schematically illustrates the placement of a metallic wire grid over the patient's scalp, with the metallic ring of the device of FIG. 9 being shown in dashed lines as it would be seen in a subsequent en face X-ray of the patient's scalp for purposes of locating the receptacle.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

In FIG. 1 the coronal portion of the head of a human patient is shown and generally designated by the numeral 10. The patient's scalp 12 overlies the skull 14 within which is seen the brain 16. A tumor 18 is schematically illustrated within the brain tissue 16. The scalp 12 has been laid back as indicated at 20 and one or more burr holes have been cut to allow creation of a bone flap (not shown) which is removed to form an access opening 22 in the skull thus providing operative access to the brain 16 and the tumor 18.

In FIG. 2, the bulk of the tumor 18 has been operatively removed thus leaving a cavity 24 within the remaining brain tissue 16 which will include some residual tumor immediately surrounding the cavity 24.

In FIG. 3, the implantable treatment apparatus 26 has been intra-operatively implanted prior to closure of the surgical incisions. The apparatus 26, as better seen in FIG. 5, includes an inflatable balloon 28 constructed for placement in the cavity 24, a subcutaneously implantable treatment fluid receptacle means 30, and a catheter means 32 connected between the receptacle means 30 and the balloon 28 for carrying treatment fluid from the receptacle means 30 to the inflatable balloon 28.

The assembly of the implantable apparatus 26 is generally as follows starting with the subcutaneous receptacle 30 and moving distally. The various connections discussed in the following description are not shown in detail in the figures, but comprise conventional widely acceptable neurosurgical techniques and will be well understood by those skilled in the art. An outlet connector extends outwardly from the subcutaneous receptacle 30 and engages an end of the siliconized plastic surgical tubing comprising the catheter 32 in a manner like that shown in FIG. 7 of U.S. Pat. No. 4,681,560 to Schulte et al., the details of which are incorporated herein by reference. The end of the outlet connector from the subcutaneous receptacle 30 includes a flange portion which sealingly engages a suture sleeve to form a seal preventing medication from exiting the

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assembly other than through the connector leading to the catheter 32.

In order for the catheter 32 to make the right-angle turn downward through burr hole 36 as illustrated in FIG. 5, a plastic right-angle device (not shown) which causes the catheter tube 32 to be conformed to a right angle can be placed around the tube at the time of installation at the proper linear dimension along the tube. Thus, depending upon the necessary distance between the subcutaneous receptacle 30 and the burr hole 36, the right-angle device may be located closer to or further from the subcutaneous receptacle 30. These assembly techniques just described confer considerable flexibility in the placement and installation of the various components of the treatment device 26.

In FIG. 3, the apparatus 26 has been implanted with the balloon 28 located within cavity 24 but still in its uninflated state. The access opening 22 has been closed by replacement of the previously removed bone flap. The catheter means 32 is placed through a burr hole 36 which may have been formed when the bone flap was formed, or which may be specially formed in any desired location. The subcutaneous receptacle 30 has been placed on top of the skull 14 and the scalp 12 has been sutured back in place thereover. The receptacle 30 may include a suture tab such as 38 (see FIG. 5) allowing it to be sutured in place to the surrounding galea which is a tough overlying tissue which lies over the skull 14.

In FIG. 4 a hypodermic needle 40 is illustrated as transdermally injecting a treatment fluid into the subcutaneously implanted receptacle 30. The injection receptacle 30 includes a rigid base and an overlying self-sealing dome which encloses and defines an injection chamber. The self-sealing dome is constructed of a silicone elastomer material, such materials providing an acceptable level of tissue reaction when subcutaneously implanted, which can be pierced by a 25 gauge or smaller needle without affecting ability of the dome to reseal after the needle is withdrawn. The fluid from needle 40 flows through the catheter 32 to inflate the balloon 28 so that it substantially fills the cavity 24 thus placing the treatment fluid in close proximity to the remaining tumor in the brain tissue 16 surrounding the cavity 24. The walls of balloon 28 can generally be described as being in direct apposition with the remaining residual tumor tissue surrounding cavity 24. As further described below, various treatment modalities may be applied either individually or simultaneously.

The Embodiment of FIG. 5

FIG. 5 illustrates the apparatus 26 in a view similar to that of FIG. 4 but enlarged and showing further detail.

The subcutaneously implanted receptacle means 30 is constructed in a manner so that it can be easily and safely injected with the treatment fluid, and it is constructed of a material which will readily reseal upon withdrawal of the hypodermic needle. It may for example be constructed similarly to the subcutaneously implantable infusion reservoir shown and described in Schulte et al., U.S. Pat. Nos. 4,816,016 and 4,681,560, the details of which are incorporated herein by reference. It may also be an Ommaya CSF Reservoir such as is available from American Heyer-Schulte. The design of the subcutaneously implantable reservoir 30 should be small enough to minimize the volume of radioactive treatment fluid 44 in the subcutaneous area, but should be large enough to allow easy localization by palpation to facilitate loading with the hypodermic syringe 40.

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The subcutaneous receptacle 30 should be malleable and flexible to allow external palpation, but should be rigid enough that external compression cannot drive fluid from its interior into the catheter 32 and balloon 28. If compression should occur, the resilience of subcutaneous receptacle 30 should provide for re-expansion, thus re-accumulating any fluid driven distally as noted above.

The catheter means 32 is constructed of conventional flexible plastic catheter materials.

The inflatable balloon 28, which may also be referred to as a distensible reservoir 28 or distensible catheter 28, is preferably constructed of flexible siliconized plastic and is attached to the catheter means 32 at location 42 by a flanged plastic connector and multiple interrupted surgical ties.

Although the term "balloon" is used to describe the distensible reservoir 28, it will be appreciated that the material from which the balloon wall is constructed need not be an elastic material. It is only required that the reservoir 28 be capable of somewhat collapsing in size so that it can be easily placed in cavity 24 as shown in FIG. 3 and that it then subsequently fill with fluid so as to substantially fill the cavity 24. The fluid inside balloon 28 is not necessarily pressurized, although it may be. The collapse of the balloon 28 following treatment will allow easy removal of the catheter 32 and balloon 28 through an existing burr hole 36 without first removing the entire bone flap should removal of the device be required for any reason.

In one preferred embodiment the treatment fluid 44 is a radioactive treatment fluid. The radioactive treatment fluid can be injected into the balloon 28 and left there for a prescribed period of time. Then it may be removed by reinserting hypodermic needle 40 into receptacle 30 and pulling a vacuum with the plunger of hypodermic needle 30 to cause the treatment fluid to flow back out of balloon 28 through catheter 32 into receptacle 30 and into the cylinder of hypodermic needle 40, so as to end the radiation treatment. Preferred radioactive isotopes for use in this procedure include 90-Yttrium, 198-Gold, 32-Phosphorous, 125-Iodine and 131-Iodine. The use of isotopes in liquid form allows considerable flexibility in administered dose rate in rad/hour and range (in millimeters) of the radioactive particles used in irradiating the residual tumor. Also with this apparatus a much more homogeneous dosage of radiation is applied to the surrounding tissue 16 than with the typical prior art devices described.

It is noted that since the apparatus 26 can be loaded with radioactive solution after the completion of surgery there is much less danger of radiation exposure to operating room personnel than with the prior art techniques described above.

Of course for treatment with radioactive fluid 44, the balloon 24 would be made of non-porous material. For other treatment modalities, namely chemotherapy, a balloon 28 constructed of porous material may be utilized in a manner similar to that described below with regard to the porous outer wall 28A of FIG. 7, in order to allow the chemotherapy fluids to seep through the balloon 28 into actual contact with the surrounding brain tissue. When a porous balloon wall 28 is used for chemotherapy, so that there is no need to ever withdraw the treatment fluid from the balloon 28, the treatment device 26 may further include a check valve (not shown) disposed in catheter 32 similar to valve 82 of

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FIG. 7 so that fluid can flow to balloon 28 but not back therefrom.

It is noted that the inflatable balloon 28 is preferably constructed so that it has an inflated volume as seen in FIG. 5 which is no greater than, and preferably slightly less than, the volume of the cavity 24 thus providing a means for avoiding any compression or distortion of the normal brain tissue 16 surrounding the cavity 24. It will be appreciated, of course, that distortion of the normal brain tissue can cause undesired complications.

FIG. 5 also illustrates a first form of heating means 46 operatively associated with the balloon means 28 for non-invasive heating of the treatment fluid 44 while the treatment fluid 44 is in the balloon 28. The heating means 46 illustrated in FIG. 5 may either be an external ultrasonic transmission means 46 or an external radio frequency electromagnetic energy transmission means 46.

If the heating means 46 is an external ultrasonic transmission means, it focuses ultrasonic energy on the treatment fluid 44 in balloon 28. In the case of using ultrasonic energy to heat the balloon contents, the skull bone tissue 14 will not be replaced over the burr hole 22 thus providing a path for unimpeded transmission of the ultrasonic sound energy through the burr hole 22.

If the heating means 46 is an external radio frequency electromagnetic energy transmission means, the treatment fluid 44 will contain an iron oxide suspension in addition to the radioactive isotope in solution. This iron oxide suspension will be heated by the radio frequency electromagnetic energy.

A monitoring means 48 is provided for monitoring a temperature of the treatment fluid 44 within the balloon means 28. In a preferred embodiment, the monitoring means 48 is a crystal oscillator 48 implanted within the balloon means 28. The oscillator 48 may also be mounted on the outside of catheter 32 within balloon 28. The crystal oscillator 48 has a frequency of oscillation which varies proportionately to its temperature. The frequency of oscillation of the crystal oscillator means 48 can be determined non-invasively by an external antenna 50 which may be considered to be a part of the monitoring means. The crystal oscillator 48 is available under the trade name CorTemp from Human Technologies, Inc., of St. Petersburg, Fla., such as described in "NASA Tech Briefs", June, 1990, at page 106, the details of which are incorporated herein by reference.

The system shown in FIG. 5, when using a non-porous balloon 28, provides a means for simultaneous application of both radioactive therapy and heat therapy to the remaining brain tissue 16 surrounding the cavity 24.

In its broadest aspects, the surgical procedure utilizing the apparatus of FIG. 5 can be described as including steps of surgically removing at least a portion of the tumor 18 thereby creating the cavity 24 in the remaining brain tissue 16. Subsequently the treatment device 26, 28 is placed in the cavity 24 and the remaining tissue 16 including residual tumor surrounding the cavity 24 is treated by means of the treatment device 26, 28. The treatment device 28 preferably is an inflatable balloon 28. The inflatable balloon is inflated with a treatment fluid 44 so that the inflatable device 28 occupies the cavity 24 thereby placing the treatment fluid 44 in close proximity to the remaining tissue 16 surrounding the cavity 24. By use of the subcutaneously implanted receptacle 30 and transdermal injections of treatment fluid as indicated in FIG. 4, the procedure can be per-

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formed non-invasively without making further surgical incisions on the patient. Although the apparatus and process of the present invention have been disclosed in the context of treatment of brain tumors, it will be appreciated that they can be used in connection with other types of tumors wherein treatment can be accomplished by placing the treatment device in a cavity left by removal of the tumor.

The entire apparatus 26 can be left in place permanently allowing subsequent further treatment as desired.

The Embodiment Of FIG. 6

FIG. 6 illustrates an alternative embodiment providing a different means for heating the treatment fluid 44 within the balloon 28.

The system shown in FIG. 6 utilizes an external microwave transmitter 52, and a subcutaneously implantable microwave receiver means 54. The microwave transmitter 52 preferably operates in the 200 MHz to 400 MHz range, and more preferably operates at about 300 MHz. The microwave receiver means 54 includes a metallic element 56 which actually receives the microwave energy and heats up. The microwave transmitter 52 may also be replaced by an ultrasound transmitter focused on receiver means 54. Insulation 58 both overlies and underlies the metallic element 56 to prevent heating of the scalp 12 and underlying skull tissue 14. Suture tabs 60 may be used to attach the microwave receiver apparatus 54 to the skull 14.

A conductor means 62 extends from the metallic element 56 into the interior of the balloon 28 for conducting heat from the metallic element 56 into the treatment fluid 44 in the balloon 28. The conductor means 62 has external insulation 64 which covers a metallic conductor 66 a portion of which uncovered inside of the balloon 28. Alternatively, the conductor means 62 could be run through the hollow catheter 32.

The system of FIG. 6 may also use a temperature monitoring means 48, 50 as shown in FIG. 5.

The Embodiment Of FIG. 7

FIG. 7 shows another alternative embodiment of the invention wherein the balloon is a double-wall balloon having a non-porous inner wall 28A, and a porous outer wall 28B. The first subcutaneously implantable receptacle 30 and catheter 32 previously described communicate with the non-porous inner wall 28A for providing the first treatment fluid 44 to the interior of the inner wall 28A. The first treatment fluid 44 is preferably a radioactive treatment fluid. The heating means 46 previously described is provided for non-invasive heating of the first treatment fluid 44. The alternative heating means of FIG. 6 could also be utilized.

A second subcutaneously implantable receptacle means 68 is provided for receiving a transdermal injection of a second treatment fluid 70, which preferably is a chemotherapy treatment fluid 70. The second receptacle 68 may be held in place by suture tabs such as 69. A second catheter 72 communicates the second receptacle 68 with the space 74 defined between the inner and outer walls 28A and 28B within which the chemotherapy fluid 70 is received. The space 74 preferably has a layer of sponge-like material 76 lying therein between the inner and outer walls 28A and 28B for temporarily holding the chemotherapy fluid 74 therein.

The porous outer wall 28B includes numerous small openings 78 therein allowing the chemotherapy fluid 74 to seep out such as in droplets 80. The chemotherapy

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fluid seeps out the porous outer wall 28 into direct contact with the brain tissue 16 surrounding the cavity 24.

The previously described crystal oscillator 48 may be placed within either the inner wall 28A or within the outer wall 28B for monitoring of the temperature of the fluids therein as previously described.

A check valve 82 may be disposed in the second catheter 72 for preventing flow of the chemotherapy fluid 70 back therethrough from space 74 back to receptacle 68. The one-way check valve 82 is available from Halkey-Roberts Corporation of St. Petersburg, Fla., and may for example be constructed in accordance with the teachings of U.S. Pat. No. 4,681,132 to Lardner, the details of which are incorporated herein by reference.

It will be appreciated that fluid pressures both from the first fluid 44 within the inner wall 28 and the second fluid 70 within the space 74 will act to urge the second fluid 70 out through the small openings 78 in the porous outer wall 28B.

FIG. 7 illustrates a treatment means including heating means 46 and the first and second subcutaneous receptacles 30 and 68 operably associated with the balloon means 28A, 28B for simultaneously non-invasively applying at least two, and if preferred all three, treatment modalities from the group consisting of radiation, heat and chemotherapy to remaining brain tissue 16 surrounding the cavity 24.

Alternatively, instead of use of a double-wall balloon 28A, 28B, chemotherapy alone could be applied with a structure like that shown in FIG. 5 wherein the outer wall 28 is a porous wall and wherein the interior thereof contains a sponge-like material.

The Embodiment Of FIG. 8

FIG. 8 illustrates a balloon 28 like that of FIG. 5, and also illustrates the fact that certain aspects of the present invention can be achieved without the use of the subcutaneously implanted receptacle 30, but instead by having a transdermal catheter 84 extend through the skull 14 and scalp 12 by means of a hollow bolt 86 implanted in the skull 14 which has the transdermal catheter 84 sealingly and securely disposed therethrough. The hollow bolt 86 may if desired be made of non-metallic materials.

The Embodiment Of FIGS. 9 And 10

FIGS. 9 and 10 illustrate another embodiment of the invention. In FIG. 9 a modified subcutaneously implantable receptacle 88 is illustrated. It is connected to balloon 28 by catheter 32.

It will be appreciated that the subcutaneously implantable reservoir 30 shown in FIGS. 1-7 is designed such that the overlying scalp 12 is somewhat deformed to accommodate the size of the subcutaneous receptacle 30. The subcutaneous receptacle 30 of FIGS. 1-7 is typically located by palpation of the scalp 40 so as to locate the subcutaneous reservoir 30 by feel. It will be appreciated that a palpable receptacle such as receptacle 30 implies pressure upon the overlying scalp 12 which may compromise blood supplied to the scalp 12 in that area, hence potentially causing skin necrosis or breakdown, a definite disadvantage.

The modified receptacle 88 is circular in shape and includes an annular metallic ring 90 which is impenetrable by X-rays. The receptacle 88 and metallic ring 90 are placed within a counterbore 92 which is formed within the skull 14 with commonly utilized air-driven

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drills such as that manufactured by the Midas Rex Company. The receptacle 88 may be held in place by suture tabs 94. It may also be held in place by conventional threaded screws (not shown) screwed into the skull 14.

The modified receptacle 88 may be installed in such a manner so as not to deform the overlying scalp 12 or create undue pressure upon the scalp 12. It does, however, present a need for an easy means of accurately locating the subcutaneous receptacle 88 so that treatment fluids may be injected therein with a hypodermic 40 similar to the process illustrated in FIG. 4. This localization is accomplished as shown in FIG. 10.

A metallic grid 94 is laid in place over the patient's scalp 12 and may be held fixedly in place thereon by means such as tape 96. Next, a plain en face radiograph, i.e., X-ray, of scalp, reservoir, grid and skull is taken. By observing the X-ray film, the relationship between the external metallic grid 94 and the subcutaneous metallic ring 90 may be easily seen, allowing selection of the correct grid square externally through which the hypodermic needle 40 can be successfully passed to hit the center of the subcutaneous receptacle 88.

Thus it is seen that the apparatus and methods of the present invention readily achieve the ends and advantages mentioned as well as those inherent therein. While certain preferred embodiments of the invention have been illustrated and described for purposes of the present disclosure, numerous changes may be made by those skilled in the art which changes are encompassed within the scope and spirit of the present invention as defined by the appended claims.

What is claimed is:

1. A surgical procedure for treating a brain tumor in a living patient, comprising:

- (a) surgically removing at least a portion of said tumor thereby creating a cavity in the patient's remaining tissue;
- (b) placing an inflatable treatment device in said cavity; and
- (c) treating remaining tissue surrounding said cavity by means of said inflatable treatment device by inflating said inflatable treatment device with a treatment fluid so that the inflatable treatment device occupies said cavity thereby placing said treatment fluid in close proximity to said remaining tissue surrounding said cavity said treating including inflating said inflatable treatment device to a volume not substantially greater than a volume of said cavity thereby avoiding any substantial compression or distortion of normal brain tissue.

2. The procedure of claim 1, wherein:

said step (c) includes treating said remaining tissue without making further surgical incisions on the patient.

3. The procedure of claim 1, wherein;

said step (c) includes applying radiation to said remaining tissue surrounding said cavity by including radioactive material in said treatment fluid in said inflatable treatment device.

4. The procedure of claim 1, wherein:

said step (c) includes simultaneously applying heat and radiation to said remaining tissue surrounding said cavity by including radioactive material in said treatment fluid in said inflatable treatment device and heating said treatment fluid including said radioactive material in said inflatable treatment device.

5. The procedure of claim 1, wherein:

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said step (c) includes simultaneously applying heat and chemotherapy to said remaining tissue surrounding said cavity by means of said inflatable treatment device.

6. The procedure of claim 1, wherein:

said step (c) includes simultaneously applying radiation and chemotherapy to said remaining tissue surrounding said cavity by means of said inflatable treatment device.

7. The procedure of claim 1, wherein:

said step (c) includes simultaneously applying heat, radiation and chemotherapy to said remaining tissue surrounding said cavity by means of said inflatable treatment device.

8. The procedure of claim 1, wherein:

in said step (b) said inflatable treatment device is connected by a catheter to an injection receptacle; and

said procedure further includes a step of implanting said injection receptacle subcutaneously.

9. The procedure of claim 8, wherein;

said step (c) includes transdermally injecting a treatment fluid into said subcutaneous injection receptacle, then flowing said treatment fluid from said injection receptacle through said catheter into said inflatable treatment device to inflate said inflatable treatment device with said treatment fluid.

10. The procedure of claim 9, wherein:

said injecting is performed with a hypodermic needle.

11. The procedure of claim 8, said tumor being a brain tumor, wherein:

said implanting of said injection receptacle includes implanting said injection receptacle between the patient's skull and scalp, with said catheter running through a hole in the patient's skull.

12. The procedure of claim 11, wherein:

said injection receptacle is recessed within a counter-bore in the patient's skull.

13. The procedure of claim 12, further comprising:

locating said injection receptacle by X-raying the patient's skull.

14. A surgical procedure for treating a tumor in a living patient, comprising:

(a) surgically removing at least a portion of said tumor; and

(b) simultaneously applying radiation, heat and chemotherapy treatment to remaining tissue surrounding a location from which said tumor was removed, without making any further surgical incisions on the patient;

wherein said step (b) is performed by placing fluid in a distensible catheter implanted during step (a) in said location from which said tumor was removed; and

wherein said fluid is placed in said distensible catheter by subcutaneously injecting said fluid into a receptacle communicated with said catheter.

15. The procedure of claim 14, wherein said tumor is a brain tumor.

16. An implantable apparatus for treatment of tissue surrounding a cavity left by surgical removal of a tumor from a living patient, comprising:

an inflatable balloon constructed for placement in said cavity;

a treatment fluid receptacle means for receiving a transdermal injection of a treatment fluid;

a catheter means, connected between said receptacle means and said balloon, for carrying said treatment

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fluid from said receptacle means to said inflatable balloon; and
 heating means, operatively associated with said balloon, for heating said treatment fluid while said treatment fluid is in said balloon and without having any electrical wiring running into said balloon. 5
 17. The apparatus of claim 16, further comprising: valve means, connected to said catheter between said balloon and said receptacle means, for controlling flow of said treatment fluid between said receptacle means and said balloon. 10
 18. The apparatus of claim 16, wherein: said inflatable balloon has an inflated volume no greater than a volume of said cavity and thus comprises a means for avoiding any compression or distortion of normal tissue surrounding said cavity. 15
 19. The apparatus of claim 16, wherein: said receptacle means is a subcutaneously implantable receptacle means.
 20. The apparatus of claim 16, wherein: 20
 said balloon means is a double-walled balloon means having an inner balloon wall received within an outer balloon wall, said inner balloon wall being non-porous for receiving and holding a radioactive fluid in an interior thereof, and said outer balloon wall being porous for receiving a chemotherapy fluid in a space between said inner and outer walls and dispersing said chemotherapy fluid through said porous outer wall. 25
 21. The apparatus of claim 20, wherein: 30
 said receptacle means is a first receptacle means for receiving said radioactive fluid, and said catheter means is a first catheter means connected between said first receptacle means and said interior of said inner balloon wall; and 35
 said apparatus further includes:
 a second treatment fluid receptacle means for receiving a transdermal injection of said chemotherapy fluid; and
 a second catheter means connected between said 40
 second receptacle means and said space between said inner and outer walls.
 22. The apparatus of claim 20, wherein: 45
 said balloon means includes a layer of sponge between said inner and outer walls.
 23. The apparatus of claim 16, further comprising: monitoring means for monitoring a temperature of said treatment fluid within said balloon means.
 24. The apparatus of claim 23, wherein: 50
 said monitoring means includes a implantable crystal oscillator having a frequency of oscillation related to its temperature and external means for sensing said frequency of oscillation of said oscillator.
 25. The apparatus of claim 16, wherein said heating means comprises: 55
 external ultrasonic transmission means for transmitting ultrasonic energy into said treatment fluid in said balloon to heat said treatment fluid.
 26. The apparatus of claim 16, wherein said heating means comprises: 60
 external radio frequency electromagnetic energy transmission means for transmitting radio frequency electromagnetic energy into said treatment fluid in said balloon to heat said treatment fluid.
 27. The apparatus of claim 16, wherein: 65
 said balloon is filled with said treatment fluid, said treatment fluid including a ferromagnetic material in suspension therein;

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said heating means includes external radio frequency electromagnetic energy transmission means for transmitting radio frequency electromagnetic energy into said treatment fluid in said balloon to heat said treatment fluid and provide heat therapy to said patient; and
 said treatment fluid further includes radioactive material so that radiation therapy is provided simultaneously with said heat therapy.
 28. An implantable apparatus for treatment of tissue surrounding a cavity left by surgical removal of a tumor from a living patient, comprising:
 an inflatable balloon means for filling at least a portion of said cavity; and
 treatment means, operably associated with said balloon means, for simultaneously applying radiation, heat and chemotherapy treatment to remaining tissue surrounding said cavity without making any further surgical incisions on the patient, wherein said treatment means further includes:
 a treatment fluid receptacle means for receiving a transdermal injection of a radioactive treatment fluid; and
 a catheter means, connected between said receptacle means and said balloon means, for carrying said radioactive treatment fluid from said receptacle means to said inflatable balloon means.
 29. A treatment apparatus for applying simultaneous heat treatment and radiation treatment to remaining tissue surrounding a cavity left by surgical removal of a tumor from a living body, comprising:
 a distensible reservoir constructed for placement in said cavity;
 a treatment fluid filling said distensible reservoir, said reservoir being distended by said treatment fluid so that said treatment fluid is in close proximity to said remaining tissue, said treatment fluid including a mixture of ferromagnetic material and radioactive material;
 catheter means for conducting said treatment fluid into said reservoir after said reservoir is placed in said cavity; and
 external radio frequency electromagnetic energy transmission means for transmitting radio frequency electromagnetic energy into said treatment fluid in said reservoir to heat said treatment fluid.
 30. The apparatus of claim 29, further comprising:
 a subcutaneously implantable treatment fluid receptacle means for receiving a transdermal injection of said treatment fluid, said receptacle means being connected to said catheter means.
 31. The apparatus of claim 29, further comprising: monitoring means for monitoring a temperature of said treatment fluid within said reservoir.
 32. The apparatus of claim 31, wherein:
 said monitoring means includes an implantable crystal oscillator and external means for sensing a frequency of oscillation of said oscillator.
 33. An implantable apparatus for treatment of tissue surrounding a cavity left by surgical removal of a tumor from a living patient, comprising:
 an inflatable balloon constructed for placement in said cavity;
 a treatment fluid receptacle means for receiving a transdermal injection of a treatment fluid, said receptacle means being at least in part impenetrable by X-rays and being constructed to be countersunk within the patient's skull;

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a catheter means connected between said receptacle means and said balloon, for carrying said treatment fluid from said receptacle means to said inflatable balloon; and

a metallic grid constructed to be temporarily attached to the patient's scalp overlying the receptacle means to permit determination of the location of said receptacle means relative to said metallic grid by X-raying the patient's skull.

34. A chemotherapy apparatus for treatment of remaining tissue surrounding a cavity left by surgical removal of a tumor from a living body, comprising:

a distensible reservoir including a porous outer wall and a non-porous inner wall arranged so that a space is defined between said inner and outer walls, and so that an interior is defined within said inner wall;

a first catheter means connected to said space between said inner and outer walls for conducting a chemotherapy fluid into said space;

sponge means disposed in said space between said inner and outer walls for temporarily holding said chemotherapy fluid;

a second catheter means connected to said interior within said inner wall for conducting a second fluid into said interior; and

first and second subcutaneously implantable fluid receptacle means, connected to said first and second catheter means, for receiving transdermal injections of said chemotherapy fluid and said second fluid, respectively.

35. A surgical procedure for treating a tumor in a living patient, comprising:

(a) surgically removing at least a portion of said tumor thereby creating a cavity in the patient's remaining tissue;

(b) placing an inflatable treatment device in said cavity; and

(c) treating remaining tissue surrounding said cavity by means of said inflatable treatment device by inflating said inflatable treatment device with a treatment fluid so that the inflatable device occupies said cavity thereby placing said treatment fluid in close proximity to said remaining tissue surrounding said cavity, said treating step including applying heat to said remaining tissue surrounding said cavity by heating said treatment fluid while said treatment fluid is contained in said inflatable treatment device without having any electrical wiring running into said inflatable treatment device.

36. A surgical procedure for treating a tumor in a living patient, comprising:

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(a) surgically removing at least a portion of said tumor thereby creating a cavity in the patient's remaining tissue;

(b) placing an inflatable treatment device in said cavity, said treatment device being connected by a catheter to an injection receptacle;

(c) implanting said injection receptacle subcutaneously;

(d) locating said injection receptacle by X-raying the patient's body; and

(e) treating remaining tissue surrounding said cavity by means of said inflatable treatment device by inflating said inflatable treatment device with a treatment fluid so that the inflatable treatment device occupies said cavity thereby placing said treatment fluid in close proximity to said remaining tissue surrounding said cavity.

37. An implantable apparatus for treatment of tissue surrounding a cavity left by surgical removal of a tumor from a living patient, comprising:

an inflatable balloon means for filling at least a portion of said cavity, said balloon means being a double-walled balloon means having an inner balloon wall received within an outer balloon wall, said outer balloon wall being porous thus providing a means for dispersing through said porous outer wall a chemotherapy fluid received in a space between said inner and outer walls; and

treatment means, operably associated with said balloon means, for simultaneously applying radiation, heat and chemotherapy treatment to remaining tissue surrounding said cavity without making any further surgical incisions on the patient.

38. An implantable apparatus for treatment of tissue surrounding a cavity left by surgical removal of a tumor from a living patient, comprising:

an inflatable balloon means for filling at least a portion of said cavity; and

treatment means, operably associated with said balloon means, for simultaneously applying radiation, heat and chemotherapy treatment to remaining tissue surrounding said cavity without making any further surgical incisions on the patient, said treatment means further including:

means for filling said balloon means with a treatment fluid;

heating means, operatively associated with said balloon means, for heating said treatment while said treatment fluid is contained in said balloon means; and

monitoring means for monitoring a temperature of said treatment fluid within said balloon means.

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 5,429,582

DATED : July 4, 1995

INVENTOR(S) : Jeffrey A. Williams

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 9, line 47, insert —step— between "treating" and "includ-".

Signed and Sealed this

Twenty-sixth Day of September, 1995

Attest:



BRUCE LEHMAN

Attesting Officer

Commissioner of Patents and Trademarks

Exhibit 11

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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

HOLOGIC, INC., CYTYC CORPORATION,
and HOLOGIC L.P.,

Plaintiffs,

vs.

SENORX, INC.,

Defendant.

AND RELATED COUNTERCLAIMS.

Case No. C08 00133 RMW (RS)

**PLAINTIFFS' DISCLOSURE OF ASSERTED
CLAIMS AND PRELIMINARY
INFRINGEMENT CONTENTIONS UNDER
PATENT LOCAL RULE 3-1**

Plaintiffs' Disclosure of Asserted Claims and
Preliminary Infringement Contentions
Case No. C08 00133 RMW (RS)

1 Plaintiffs Hologic, Inc, Cytac Corporation, and Hologic L.P. (collectively, “Hologic”), by
2 counsel and pursuant to Patent Local Rule 3-1 of this Court, hereby submits its disclosure of asserted
3 claims and preliminary infringement contentions relating to U.S. Patents Nos. 5,913,813 (the “‘813
4 patent”), 6,413,204 (the “‘204 patent”), and 6,482,142 (the “‘142 patent”). Hologic reserves the right
5 to supplement or amend its identification of asserted claims, accused instrumentalities and
6 infringement contentions contained herein (a) based on additional information concerning Defendant
7 SenoRx, Inc.’s (“SenoRx”) products and methods obtained through discovery or other means, (b) as
8 appropriate, in response to the Court’s determination of legal issues, including without limitation the
9 construction of disputed terms, phrases and clauses identified by either party, or (c) for any other good
10 cause shown. See Pat. L.R. 3-6 & 3-7.

11 **I. INFRINGEMENT CHARTS FOR EACH ASSERTED CLAIM (Patent L.R. 3-1(c))**

12 **A. U.S. Patent No. 5,913,813**

13 Attached as Appendix A is a chart identifying specifically where each element of each
14 asserted claim of the ‘813 patent (claims 11 and 12) is found within SenoRx’s Contura™ Multi-Lumen
15 Balloon Source Applicator for Brachytherapy, models B001-45 and B011-45.

16 **B. U.S. Patent No. 6,413,204**

17 Attached as Appendix B is a chart identifying specifically where each element of each
18 asserted claim of the ‘204 patent (claims 4 and 17) is found within SenoRx’s Contura™ Multi-Lumen
19 Balloon Source Applicator for Brachytherapy, models B001-45 and B011-45. Each asserted claim is
20 entitled to a priority date of July 4, 1997.

21 **C. U.S. Patent No. 6,482,142**

22 Attached as Appendix C is a chart identifying specifically where each element of each
23 asserted claim of the ‘142 patent (claims 1, 6, and 8) is found within SenoRx’s Contura™ Multi-
24 Lumen Balloon Source Applicator for Brachytherapy, models B001-45 and B011-45. The first two
25 claim elements of claim 1 (as tabled in Appendix C) are entitled to a priority date of July 4, 1997.

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D. Materials Relied Upon

Attached as Appendix D is a list of exemplary materials that provide factual support for Hologic's infringement contentions, as set forth herein and in Appendices A, B, and C. While sufficient on their own to establish infringement, the materials appearing on this list are not intended to be the complete factual record on which Hologic will rely to prove infringement at trial.

**II. RELIANCE ON OWN PRODUCTS AS PRACTICING THE CLAIMED INVENTION
(Patent L.R. 3-1(f))**

Hologic intends to rely upon its own products, namely, the Mammosite® Radiation Therapy System, as practicing the inventions of each and every asserted claim of the '813 and '204 patents.

Dated: May 6, 2008

HOWREY LLP

By: Katharine L. Altemus
Katharine L. Altemus

HOWREY LLP
Attorneys for Plaintiffs
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PROOF OF SERVICE

I am employed in the County of San Mateo, State of California. I am over the age of 18 and not a party to the within action. My business address is 1950 University Avenue, 4th Floor, East Palo Alto, California 94303.

On May 6, 2008, I served on the interested parties in said action the within:

PLAINTIFFS' DISCLOSURE OF ASSERTED CLAIMS AND PRELIMINARY INFRINGEMENT CONTENTIONS UNDER PATENT LOCAL RULE 3-1 with APPENDIX A, APPENDIX B, APPENDIX C, and APPENDIX D

by placing a true copy thereof in a sealed envelope(s) addressed as stated below and causing such envelope(s) to be deposited in the U.S. Mail at East Palo Alto, California.

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Washington, D.C. 20005


☒ (MAIL) I am readily familiar with this firm's practice of collection and processing correspondence for mailing. Under that practice it would be deposited with the U.S. postal service on that same day in the ordinary course of business. I am aware that on motion of party served, service is presumed invalid if postal cancellation date or postage meter date is more than 1 day after date of deposit for mailing in affidavit.

☒ (EMAIL/ELECTRONIC TRANSMISSION) Based on a court order or an agreement of the parties to accept service by e-mail or electronic transmission, I caused the documents to be sent to the persons at the e-mail addresses listed above. I did not receive, within a reasonable time after the submission, any electronic message or other indication that the transmission was unsuccessful.

I declare under penalty of perjury that I am employed in the office of a member of the bar of this Court at whose direction the service was made and that the foregoing is true and correct.

Executed on May 6, 2008, at East Palo Alto, California.

Sonya Schwab
(Type or print name)


(Signature)

Appendix A

APPENDIX A
INFRINGEMENT CLAIMS OF U.S. Patent No. 5,913,813

Asserted Claim¹	Contura™ Multi-Lumen Balloon Source Applicator²
<p><i>1. Apparatus for delivering radioactive emissions to a body location with a uniform radiation profile, comprising:</i></p>	<p><u>CONTENTION:</u></p> <p>The Contura™ Multi-Lumen Balloon Source Applicator (“Contura™”) (formerly marketed under the product name SenoRad) is an interstitial brachytherapy apparatus designed to deliver intracavity radiation to the margins of the cavity remaining after surgical resection of breast cancer.</p> <p>SenoRx Inc. (“SenoRx”) makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 1 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-</p>

¹ Asserted Claims 11 and 12 depend from unasserted Claims 1, 2, and 8 (for which, therefore, the elements are matched to features of the accused instrumentality).

² The “Support” cited herein is exemplary, and although sufficient to support a claim of infringement, is not the complete factual record on which Hologic intends to rely to prove infringement at trial. To the extent that further discovery shows any element of an asserted claim is not present literally, Hologic will rely at least on the identified evidence to show that the element is present under the doctrine of equivalents.

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	<p>HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad Multi-Lumen Balloon Source Applicator for Brachytherapy is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.” Ref. No. 2 at 2232.</p> <p>“SenoRx, Inc. (NASDAQ:SENO) today announced that it has launched Contura™, its Multi-Lumen Balloon (MLB) Catheter for delivering brachytherapy to the surgical margins following lumpectomy for breast cancer.” Ref. No. 5.</p> <p>See also evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See also Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35 ; Ref. No. 36 ; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38 ; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.
(a) a catheter body member having a proximal end and distal end;	<p><u>CONTENTION:</u></p> <p>The Contura™ has a catheter with a proximal and distal end, with proximal ports for inflation and vacuum, as well as a distal “vacuum port.” “Radiation source lumens” also run from the proximal end of the applicator into the treatment lumens at the distal end of the catheter. This claim element is thus <u>literally</u> infringed.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator consists of a multi-lumen catheter attached to an inflatable spherical balloon (Figure 1).” Ref. No. 2 at 2232.</p> <p>Illustrations of the SenoRx Multi-Lumen Balloon Source Applicator show a catheter with a proximal and distal end, with proximal ports for inflation (“inflation luer”) and vacuum (“vacuum luer”), as well as a distal “vacuum port”. “Radiation source lumens” are also run from the proximal end of the applicator into the treatment lumens at the distal end of the catheter. Ref. No. 2 at Figure 1; Ref. No. 3.</p> <p>“Two proximal ports are also provided with Luer-type connectors for balloon inflation/deflation and for application of intracavitary vacuum.” Ref. No. 2 at 2232.</p> <p>See generally Ref. No. 4.</p> <p>See <i>a/so</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte's Order Denying Plaintiffs' Motion For Preliminary Injunction.
(b) an inner spatial volume disposed proximate the distal end of the catheter body member;	<p><u>CONTENTION:</u></p> <p>Each of the five treatment lumens inside the Contura™ balloon comprises a region of space surrounded by an outer spatial volume and enclosed by a polymeric film wall and therefore embodies an inner spatial volume proximate to the distal end of the Contura™ catheter. Ref. No. 24 at 28. Alternatively, the radionuclide itself comprises a region of space surrounded by an outer spatial volume and defined by the outside surface of a solid radionuclide sphere and therefore embodies an inner spatial volume. Id. This claim element is thus <u>literally</u> infringed.</p> <p>Alternatively, the five treatment lumens and the area within the balloon between and surrounding those lumens are insubstantially different from a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere. They function in substantially the same way (controlled positioning of a radiation source within the outer spatial volume) to provide substantially the same result (delivery of a prescribed radiation dose to target tissue). This claim element is thus infringed under the <u>doctrine of equivalents</u>.</p> <p><u>SUPPORT:</u></p> <p>Ref. No. 24 at 28.</p> <p>“Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen.” Ref. No. 1 at Device description.</p> <p>“Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen.” Ref. No. 2 at page 2.</p> <p>An illustration of the Contura™ applicator shows the five treatment lumens within Ref. No. 3.</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	<p>See generally Ref. No. 4 (showing 4 “offset” lumen).</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p>
<p><i>(c) an outer, closed, inflatable, chamber defined by a radiation transparent wall affixed to the body member proximate the distal end thereof in surrounding relation to the inner spatial volume with a predetermined constant spacing between said inner spatial volume and the radiation transparent wall;</i></p>	<p><u>CONTENTION:</u></p> <p>The central treatment lumen is located within the balloon (i.e., the “outer, closed, inflatable chamber defined by a radiation transparent wall:”) along the longitudinal axis of the applicator.</p> <p>The Contura™ inflatable balloon is an “outer, closed, inflatable, chamber”), and is affixed proximate to the vacuum port at the distal end of the applicator catheter. The surface of the expandable balloon (“a radiation transparent wall”) defines the outer spatial volume of the balloon applicator. The Contura™ balloon surrounds and contains the inner spatial volume(s) discussed above. The spacing (predetermined by one of skill in the art) between the inner spatial volume and the wall of the Contura™ balloon is constant. This claim element is thus <u>literally</u> infringed.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire.” Ref. No. 1 at Device description.</p> <p>“Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator consists of a multi-lumen catheter attached to an inflatable spherical balloon (Figure 1).” Ref. No. 2 at 2232.</p> <p>“Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	<p>the central lumen.” Ref. No. 2 at page 2.</p> <p>An illustration of the Contura™ applicator shows the five treatment lumens within Ref. No. 3.</p> <p>See generally Ref. No. 4.</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p>
<p><i>(d) a material containing a radionuclide(s) disposed in one of the inner spatial volume and outer chamber; and</i></p>	<p><u>CONTENTION:</u></p> <p>Each radiation source (“radiation source wire”) is inserted through a radiation source lumen in the Contura into its respective central or curved treatment lumen. The five treatment lumens are located within the expandable outer surface of the balloon. Alternatively, each radiation source has a radionuclide surface that defines the inner spatial volume in which it is disposed. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 1 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	<p><u>SUPPORT:</u></p> <p>“The SenoRad applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available HDR (High Dose Rate) remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided, one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen.” Ref. No. 19 at SRX-HOL00005564.</p> <p>See generally Ref. No. 4.</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p>
<p><i>(e) means disposed in the other of the inner spatial volume and outer chamber for rendering uniform the radial absorbed dose profile of the emissions from the</i></p>	<p><u>CONTENTION:</u></p> <p>The Contura™ balloon is intended to be filled with a radiation absorbing or attenuating</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²						
<p><i>one of the inner spatial volume and outer chamber containing the radionuclides.</i></p>	<p>material (e.g., physiological saline or saline/contrast mixture) for making the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the balloon (“rendering uniform the radial absorbed dose profile of the emissions from the radiation source within the inner spatial volume”). This claim element is thus <u>literally</u> infringed.</p> <p><u>SUPPORT:</u></p> <p>“The balloon is inflated to a 4 or 5 cm spherical shape by a controlled volume injunction of physiological saline to approximately 33 or 58 ml. respectively.” Ref. No. 19 at SRX-HOL00005564.</p> <p>“The inflated shape allows for placement of a radiation source at the center or close to the center of the balloon to deliver doses of gamma radiation to the margins of the lumpectomy cavity.” Ref. No. 19 at SRX-HOL00005564</p> <p>“Inflate balloon with saline/contrast mixture” Ref. No. 17 at SRX-HOL00006650.</p> <p>“The balloon is then inflated to a 4 to 6 cm spherical shape by a controlled volume injection of physiological saline.” Ref. No. 20 at SRX-HOL00004120.</p> <p>“Contrast media concentration of less than 10% are recommended to prevent dose attenuation.” Ref. No. 2 at 2232.</p> <p>“8. Using the syringes provided, inflate the Applicator balloon with the contrast media solution to the desired fill volume. Purge any air from the fill syringes before attaching them to the Applicator.”</p> <table data-bbox="1087 1110 1780 1201"> <tr> <td>Desired balloon diameter</td><td>Approximate balloon fill volume</td></tr> <tr> <td>4 cm</td><td>33 ml</td></tr> <tr> <td>5 cm</td><td>58 ml</td></tr> </table> <p>Ref. No. 2 at 2232.</p> <p>See also Ref. No. 16 at SRX-HOL00006598.</p> <p>See generally Ref. No. 4.</p>	Desired balloon diameter	Approximate balloon fill volume	4 cm	33 ml	5 cm	58 ml
Desired balloon diameter	Approximate balloon fill volume						
4 cm	33 ml						
5 cm	58 ml						

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	See <i>also</i> evidence attached to Plaintiffs' Motion For Preliminary Injunction, Plaintiffs' Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte's Order Denying Plaintiffs' Motion For Preliminary Injunction.
<p>2. The apparatus as in claim 1 wherein said inner spatial volume is an inner closed, chamber defined by a further radiation transparent wall.</p>	<p><u>CONTENTION:</u></p> <p>Each of the five treatment lumens inside the Contura™ balloon comprises a region of space, which is an inner, closed chamber, surrounded by an outer spatial volume and enclosed by a radiation transparent, polymeric film wall. Each of the five treatment lumens thus embodies an inner spatial volume proximate to the distal end of the Contura™ catheter. Ref. No. 24 at 28. This claim element is thus <u>literally</u> infringed.</p> <p>Alternatively, the five treatment lumens and the area within the balloon between and surrounding those lumens are insubstantially different from a region of space that is an inner, closed chamber, surrounded by an outer spatial volume and enclosed by a radiation transparent, polymeric film wall. This claim element is thus infringed under the <u>doctrine of equivalents</u>.</p> <p>SenoRx Inc. ("SenoRx") makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 2 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	<p>HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>See Ref. No. 21.</p> <p>See generally Ref. No. 4.</p> <p>See <i>also</i> evidence attached to Plaintiffs' Motion For Preliminary Injunction, Plaintiffs' Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte's Order Denying Plaintiffs' Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>See <i>also</i> Ref. No. 24 at 28.</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
<p>8. The apparatus as in claim 2 wherein the inner chamber contains the radioactive material.</p>	<p><u>CONTENTION:</u></p> <p>Each of the five treatment lumens inside the Contura™ balloon provides an inner, closed chamber, which during use, is the structure that contains a radioactive source. Ref. No. 24 at 28. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx Inc. (“SenoRx”) makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 8 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	<p>suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The Contura™ MLB applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available HDR (High Dose Rate) remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided, one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen.” Ref. No. 19 at SRX-HOL00005564.</p> <p>See generally Ref. No. 4.</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	See also Ref. No. 24 at 28.
<p>11. The apparatus as in claim 8 wherein the radioactive material is a solid.</p>	<p><u>CONTENTION:</u></p> <p>During patient treatment, an afterloader under computer control inserts source wires with attached solid radionuclides through the radiation source wire lumens of the Contura™ device into predetermined source dwell positions within the treatment lumens (“inner chamber”) at the distal end of the device. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx Inc. (“SenoRx”) makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 11 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	<p>Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad Multi-Lumen Balloon Source Applicator for Brachytherapy is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.” Ref. No. 1 at Device description.</p> <p>“Lumens are provided for attachment to commercially available HDR (High Dose Rate) remote afterloader equipment for passage of the radiation source delivery wire.” Ref. No. 2 at 2232.</p> <p>“Afterloader compatibility: Model B001-45-VeriSource 200, VariSource ID and Nucletron HDR afterloaders. Model B011-45-GammaMedPlus afterloader (Cannot be used with GammaMed 12f).” Ref. No. 2 at 2232.</p> <p>“SenoRx, Inc. (NASDAQ:SENO) today announced that it has launched Contura™, its Multi-Lumen Balloon (MLB) Catheter for delivering brachytherapy to the surgical margins following lumpectomy for breast cancer.” Ref. No. 5.</p> <p>See generally Ref. No. 4.</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35 ; Ref. No. 36 ; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38 ; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.
<p>12. The apparatus as in claim 1 wherein the material containing a radionuclide comprises a plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile.</p>	<p><u>CONTENTION:</u></p> <p>During treatment using the Contura, the radiation source wire lumens to which the radionuclide(s) is/are attached are inserted into predetermined locations (dwell positions) within the treatment lumens at the distal end of the device. The multiple treatment lumens of the Contura™ allow multiple solid radiation sources (e.g., single radionuclide sources on multiple separate source wires) to be arrayed simultaneously within separate lumens to provide a desired composite radiation profile within the targeted tissue. Alternatively, a single solid radionuclide on a source wire can be inserted sequentially into one or more predetermined locations within multiple treatment lumens to provide a desired composite radiation profile within the targeted tissue. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx Inc. (“SenoRx”) makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 12 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	<p>SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The radiation balloon uses vacuum to remove excess air and fluid and to adhere closely to often irregularly shaped lumpectomy cavities in order to deliver precise radiation dosing through multiple seed lumens.” Ref. No. 17 at SRX-HOL00006639.</p> <p>“Each lumen can accommodate 8 dwell positions.” Ref. No. 17 at SRX-HOL00006642.</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688,</p>

Asserted Claim ¹	Contura™ Multi-Lumen Balloon Source Applicator ²
	<p>1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p><i>See also Ref. No. 21.</i></p>

Appendix B

APPENDIX B
INFRINGEMENT CLAIMS OF U.S. Patent No. 6,413,204

Asserted Claim^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator³
<p><i>1. An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:</i></p>	<p><u>CONTENTION:</u></p> <p>The Contura Multi-Lumen Balloon Source Applicator (“Contura™”) is an interstitial brachytherapy apparatus designed to deliver intracavity radiation to the margins of the cavity remaining after surgical resection of breast cancer.</p> <p>SenoRx Inc. (“SenoRx”) makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 1 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at</p>

¹ Each asserted claim is entitled to a priority date of July 24, 1997.

² Asserted Claims 4 and 17 depend from unasserted claims 1, 2, and 3 (for which, therefore, the elements are matched to features of the accused instrumentality).

³ The “Support” cited herein is exemplary, and although sufficient to support a claim of infringement, is not the complete factual record on which Hologic intends to rely to prove infringement at trial. To the extent that further discovery shows any element of an asserted claim is not present literally, Hologic will rely on at least the identified evidence to show that the element is present under the doctrine of equivalents.

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad Multi-Lumen Balloon Source Applicator for Brachytherapy is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.” Ref. No. 2 at 2232.</p> <p>“SenoRx, Inc. (NASDAQ:SENO) today announced that it has launched Contura™, its Multi-Lumen Balloon (MLB) Catheter for delivering brachytherapy to the surgical margins following lumpectomy for breast cancer.” Ref. No. 5.</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p>
<p><i>(a) a catheter body member having a proximal end and distal end;</i></p>	<p><u>CONTENTION:</u></p> <p>The Contura™ has a catheter with a proximal and distal end, with proximal ports for inflation and vacuum, as well as a distal “vacuum port.” “Radiation source lumens” also run from the proximal end of the applicator into the treatment lumens at the distal end of the catheter. This claim element is thus <u>literally</u> infringed.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator consists of a multi-lumen catheter attached to an inflatable spherical balloon (Figure 1).” Ref. No. 2 at 2232.</p> <p>Illustrations of the SenoRx Multi-Lumen Balloon Source Applicator show a catheter with a proximal and distal end, with proximal ports for inflation (“inflation luer”) and vacuum (“vacuum luer”), as well as a distal “vacuum port”. “Radiation source lumens” are also run from the proximal end of the applicator into the treatment lumens at the distal end of the catheter. Ref. No. 2 at Figure 1; Ref. No. 3.</p> <p>“Two proximal ports are also provided with Luer-type connectors for balloon inflation/deflation and for application of intracavitary vacuum.” Ref. No. 2 at 2232.</p> <p>See generally Ref. No. 4.</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	See <i>also</i> evidence attached to Plaintiffs' Motion For Preliminary Injunction, Plaintiffs' Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte's Order Denying Plaintiffs' Motion For Preliminary Injunction.
(b) an inner spatial volume disposed proximate to the distal end of the catheter body member;	<p><u>CONTENTION:</u></p> <p>Each of the five treatment lumens inside the Contura™ balloon comprises a region of space surrounded by an outer spatial volume and enclosed by a polymeric film wall and therefore embodies an inner spatial volume proximate to the distal end of the Contura™ catheter. Ref. No. 24 at 28. Alternatively, the radionuclide itself comprises a region of space surrounded by an outer spatial volume and defined by the outside surface of a solid radionuclide sphere and therefore embodies an inner spatial volume. <i>Id.</i> This claim element is thus <u>literally</u> infringed.</p> <p>Alternatively, the five treatment lumens and the area within the balloon between and surrounding those lumens are insubstantially different from a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere. They function in substantially the same way (controlled positioning of a radiation source within the outer spatial volume) to provide substantially the same result (delivery of a prescribed radiation dose to target tissue). This claim element is thus infringed under the <u>doctrine of equivalents</u>.</p> <p><u>SUPPORT:</u></p> <p>"Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen." Ref. No. 1 at Device description.</p> <p>"Five radiation source wire lumens are provided; one central lumen located along the long axis of the Applicator and four curved lumens symmetrically offset from the central lumen." Ref. No. 2 at page 2232.</p> <p>An illustration of the Contura™ applicator shows the five treatment lumens within Ref. No. 3.</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>See generally Ref. No. 4 (showing 4 “offset” lumen).</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 24 at 28.</p>
<p><i>(c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and</i></p>	<p><u>CONTENTION:</u></p> <p>The inflatable spherical balloon is an “expandable surface element”, and is located proximate to the vacuum port at the distal end of the applicator catheter. The three-dimensional surface of the expandable balloon defines the outer spatial volume of the balloon applicator. The outer spatial volume surrounds and contains the inner spatial volume(s). Each of the five treatment lumens inside the Contura™ balloon comprises a region of space surrounded by an outer spatial volume and enclosed by a polymeric film wall and therefore embodies an inner spatial volume proximate to the distal end of the Contura™ catheter. Ref. No. 24 at 28. Alternatively, the radionuclide itself comprises a region of space surrounded by an outer spatial volume and defined by the outside surface of a solid radionuclide sphere and therefore embodies an inner spatial volume. <i>Id.</i> This claim element is thus <u>literally</u> infringed.</p> <p>Alternatively, the five treatment lumens and the area within the balloon between and surrounding those lumens are insubstantially different from a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere. They function in substantially the same way (controlled positioning of a radiation source within the outer spatial volume) to provide substantially the same result (delivery of a prescribed radiation dose to target tissue). This claim element is thus infringed under the <u>doctrine of equivalents</u>.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen. The balloon is inflated to a 4 or 5 cm spherical shape by a controlled volume injection of physiological saline to approximately 32 or 55 ml, respectively.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator consists of a multi-lumen catheter attached to an inflatable spherical balloon (figure 1). Lumens are provided for attachment to commercially available HDR (High Dose Rate) remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen.” Ref. No. 2 at page 2232.</p> <p>An illustration of the Contura™ applicator shows the five treatment lumens, the outer spatial volume as defined by the expandable polyurethane balloon, and the inner spatial volume. Ref. No. 3.</p> <p>See generally Ref. No. 4 (showing expansion of balloon with subsequent increase in size of outer spatial volume)</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 24 at 28.</p>
<p><i>(d) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.</i></p>	<p><u>CONTENTION:</u></p> <p>Each radiation source (“radiation source wire”) is inserted through a radiation source lumen into its respective central or curved treatment lumen (one “central lumen” and four “curved lumens”). Each of the five treatment lumens inside the Contura™ balloon comprises a region of space surrounded by an outer spatial volume and enclosed by a polymeric film wall and therefore embodies an inner spatial volume proximate to the distal end of the Contura™ catheter. Ref. No. 24 at 28. Alternatively, the radionuclide itself comprises a region of space surrounded by an outer spatial volume and defined by the outside surface of a solid radionuclide sphere and therefore embodies an inner spatial volume. <i>Id.</i> The Contura™ balloon surrounds and contains the inner spatial</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>volume(s). Because the spacing (predetermined by one of skill in the art) between the inner spatial volume and the wall of the spherical Contura™ balloon is constant, the accused device provides a three-dimensional isodose profile generated by the radiation source that is substantially similar in shape to the balloon. This claim element is thus <u>literally</u> infringed.</p> <p>Alternatively, the five treatment lumens and the area within the balloon between and surrounding those lumens are insubstantially different from a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere. They function in substantially the same way (controlled positioning of a radiation source within the outer spatial volume) to provide substantially the same result (delivery of a prescribed radiation dose to target tissue). This claim element is thus infringed under the <u>doctrine of equivalents</u>.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 1 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad applicator consists of a multi-lumen catheter connected to an</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen. The balloon is inflated to a 4 or 5 cm spherical shape by a controlled volume injection of physiological saline to approximately 32 or 55 ml, respectively.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator consists of a multi-lumen catheter attached to an inflatable spherical balloon (figure 1). Lumens are provided for attachment to commercially available HDR (High Dose Rate) remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen.” Ref. No. 2 at page 2232.</p> <p>“In addition, the Contura MLB uses vacuum suction to remove excess seroma and air to enhance conformance of often irregularly shaped lumpectomy cavity walls to the balloon surface in order to deliver precise radiation dosing through multiple radiation source lumens.” Ref. No. 5.</p> <p>An illustration of the Contura™ applicator shows the five treatment lumens, into which the radiation source is inserted, which lumens collectively form the inner spatial volume. Ref. No. 3.</p> <p>“The Applicator red-capped radiation source wire lumens are numbered ‘1’, ‘2’, ‘3’, ‘4’ and ‘5’ and positioned as shown in Figure 3. Lumen number ‘1’ corresponds to the offset lumen closest and parallel to the longitudinal radiopaque line (M) along the outside of the catheter. Lumen number ‘5’ corresponds to the central lumen. Remove the red caps and use commercially available connectors to attach the source lumens to the afterloader.” Ref. No. 2 at 232.</p> <p>See generally Ref. No. 4 (describing insertion of the radioactive seeds into the treatment lumens).</p> <p>See generally Ref. No. 4 (showing animated depiction of the insertion of radioactive seeds into a treatment lumen).</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>See <i>also</i> evidence attached to Plaintiffs' Motion For Preliminary Injunction, Plaintiffs' Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte's Order Denying Plaintiffs' Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 24 at 28.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p>
<p>2. <i>The apparatus of claim 1, wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.</i></p>	<p><u>CONTENTION:</u></p> <p>The Contura™ Multi-Lumen Balloon Catheter is a balloon-based device which is inserted into a cavity remaining after the excision of a breast tumor. Once the balloon is in the cavity, the balloon is inflated with a contrast media or saline (injected through the inflation port) to conform the cavity to the shape of the balloon. Parameters of the balloon size and location are adjusted to conform to the surgical margin of the tissue to the shape of the outer volume of the balloon. Insertion of radiation source wires into select treatment lumens for prescribed lengths of time controls the dose of radiation targeting the tissue to be treated, thereby preventing damage to healthy tissue proximate to the surface of the balloon. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx Inc. ("SenoRx") makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 2 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“It’s a balloon-based device. The balloon is implanted into the breast and it replaces the tissue that was removed by the surgeon. And the goal of the treatment is to treat the rind of the tissue surrounding the balloon. This animation provided to us by the makers of the device shows how it works. After the balloon is inserted into the breast, it is inflated and filled with a saline solution. Then radioactive seeds are sent through five separate channels inside the balloon. The dose is actually directed by where the seed sits within the balloon. So, having one offset from the center of the balloon allows us to pull that dose by leaving the seed in the balloon for a certain period of time – longer than the other side has it for an example. And that means the dosage of the</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³						
	<p>radiation is concentrated on the tumor and doesn't burn the patient's skin. And if the skin was too close to channel 1, we might put the seed longer in channel 3 and 4 versus channel 1 to cool down that side of the dose." Ref. 4.</p> <p>"In addition, the Contura MLB uses vacuum suction to remove excess seroma and air to enhance conformance of often irregularly shaped lumpectomy cavity walls to the balloon surface in order to deliver precise radiation dosing through multiple radiation source lumens." Ref. No. 5.</p> <p>"8. Using the syringes provided, inflate the Applicator balloon with the contrast media solution to the desired fill volume.</p> <table data-bbox="1087 613 1780 711"> <tr> <td>Desired balloon diameter</td><td>Approximate balloon fill volume</td></tr> <tr> <td>4 cm</td><td>33 ml</td></tr> <tr> <td>5 cm</td><td>58 ml</td></tr> </table> <p>Ref. No. 2 at 2232.</p> <p>"10. Use ultrasound to confirm appropriate placement, volume and cavity conformance. Fluid and air surrounding the Applicator balloon may be aspirated with a 30 ml Syringe attached to the white Vacuum Port (N). The volume of the balloon may be adjusted through the blue Inflation Port (M). Replace Luer Caps when finished." Ref. No. 2 at 2232.</p> <p>"RADIATION DELIVERY - Refer to Figure 3</p> <p>1. CT imaging should be used in conjunction with commercially available treatment planning software to determine the appropriate source lumens, source dwell positions and dwell times for optimized radiation delivery of a prescribed dose to the targeted treatment volume.</p> <p>2. Note the orientation of the Contura™ MLB Applicator with respect to the radiopaque line on the catheter shaft. Verify correct Applicator orientation, balloon position, balloon volume, skin spacing and conformance using imaging prior to delivery of each fraction of radiation. Adjust if necessary.</p> <p>3. The Applicator red-capped, radiation source wire lumens are numbered '1', '2', '3', '4' and '5' and positioned as shown in Figure 3. Lumen number '1' corresponds to the</p>	Desired balloon diameter	Approximate balloon fill volume	4 cm	33 ml	5 cm	58 ml
Desired balloon diameter	Approximate balloon fill volume						
4 cm	33 ml						
5 cm	58 ml						

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>offset lumen closest and parallel to the longitudinal radiopaque line (M) along the outside of the catheter. Lumen number '5' corresponds to the central lumen. Remove the red caps and use commercially available connectors to attach the source lumens to the afterloader. After each treatment replace the red caps.” Ref. No. 2 at 2232.</p> <p>“Multiple offset lumens provide dose shaping opportunities to minimize skin and rib dose.” Ref. No. 3.</p> <p>“Vacuum ports enable the removal of fluid & air and facilitate tissue conformance to the balloon for more uniform dosing.” Ref. No. 3.</p> <p>See generally Ref. No. 4 showing animated depiction of the insertion and use of the Contura™ device).</p> <p>See also evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See also Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p>
<p>3. The apparatus of claim 2, wherein a predetermined spacing is provided between said inner spatial volume and the expandable surface element.</p>	<p><u>CONTENTION:</u></p> <p>The Contura™ balloon is an “expandable surface element”, and is affixed proximate to the vacuum port at the distal end of the applicator catheter. The surface of the expandable balloon defines the outer spatial volume of the balloon applicator. The</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>Contura™ balloon surrounds and contains the inner spatial volume(s) (discussed above). The spacing between the inner spatial volume and the wall of the Contura™ balloon is constant. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx Inc. (“SenoRx”) makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 3 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>See <i>also</i> evidence attached to Plaintiffs' Motion For Preliminary Injunction, Plaintiffs' Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte's Order Denying Plaintiffs' Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030..</p>
<p>4. The apparatus of claim 3, wherein the expandable surface element is adapted to contact tissue surrounding a resected cavity and adapted to conform the tissue to the desired shape of the expandable surface element.⁴</p>	<p><u>CONTENTION:</u></p> <p>Following implantation, the Contura™ balloon is inflated to contact tissue surrounding a resected cavity and to conform the tissue along the resection bed to the three-dimensional shape of the balloon. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx Inc. ("SenoRx") makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-</p>

⁴ Claim 4 of the '204 patent contains all of the limitations of claim 36 of the '204 patent (presented in the interests of clarity and economy within Plaintiffs' Motion For Preliminary Injunction as an exemplary claim infringed by SenoRx), plus the additional limitation of the expandable surface element ...adapted to contact tissue surrounding a resected cavity and conform the tissue to the desired shape of the expandable surface element.

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 4 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use..</p> <p><u>SUPPORT:</u></p> <p>“A series of drain holes at the tip of the catheter and at the proximal balloon hub allow for suction to be used to help the lumpectomy cavity conform to the balloon.” Ref. No. 20 at SRX-HOL00004120.</p> <p>“The Applicator is not intended for use in cavities that are too small, too large and/or of shapes unable to conform to an approximately spherical, 4 to 5 cm diameter SenoRx balloon.” Ref. No. 2 at SRX-HOL00002232.</p> <p>“The balloon is inflated to a 4 or 5 cm spherical shape by a controlled volume injection of physiological saline to approximately 33 or 58 ml, respectively. A series of drain holes at the tip of the catheter and at the proximal balloon hub allow for suction to be used to help the lumpectomy cavity conform to the balloon.” Ref. No. 19 at SRX-</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>HOL00005564.</p> <p>“The radiation balloon uses vacuum to remove excess air and fluid and to adhere closely to often irregularly shaped lumpectomy cavities in order to deliver precise radiation dosing through multiple seed lumens.” Ref. No.17 at SRX-HOL00006639.</p> <p>“Use ultrasound to confirm good tissue to balloon conformance and document skin spacing.” Ref. No. 17 at SRX-HOL00006650.</p> <p>“Contour anatomy and target.” Ref. No. 17 at SRX-HOL00006654.</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p>
<p>17. The apparatus of claim 1, wherein the radiation source is a plurality of solid radiation sources arranged to provide an isodose profile having a shape substantially similar to the shape of the outer spatial volume.</p>	<p><u>CONTENTION:</u></p> <p>The multiple treatment lumens of the Contura allow multiple solid radiation sources to be arrayed simultaneously within two or more separate treatment lumens to provide an isodose profile having a shape substantially similar to the shape of the balloon within the targeted tissue. Alternatively, the multiple treatment lumens of the Contura allow one or more solid radiation sources to be arrayed at different points in time within one or more separate treatment lumens to provide an isodose profile having a shape</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p>substantially similar to the shape of the balloon within the targeted tissue. Appropriate pre-treatment dosimetry planning (with multiple dwell locations, multiple dwell times and/or use of multiple lumens) allows the isodose profile to be contoured to be substantially similar to the shape to the outer spatial volume defined by circumference of the expandable balloon. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx Inc. (“SenoRx”) makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 17 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p>

Asserted Claim ^{1,2}	Contura™ Multi-Lumen Balloon Source Applicator ³
	<p><u>SUPPORT:</u></p> <p>Ref. No. 9 at SRX-HOL00006494; Ref. No. 17 at 6655-6656; Ref. No. 22 at 10, 16.</p> <p>See <i>also</i> evidence attached to Plaintiffs' Motion For Preliminary Injunction, Plaintiffs' Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte's Order Denying Plaintiffs' Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p>

Appendix C

APPENDIX C
INFRINGEMENT CLAIMS OF U.S. Patent No. 6,482,142

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
<p>1. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:</p>	<p><u>CONTENTION:</u></p> <p>The SenoRad Multi-Lumen Balloon Source Applicator (“Contura™”) is an interstitial brachytherapy apparatus designed to deliver localized radiation to the margins of the cavity remaining after surgical resection of breast cancer.</p> <p>SenoRx Inc. (“SenoRx”) makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 1 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-</p>

¹ The “Support” cited herein is exemplary, and although sufficient to support a claim of infringement, is not the complete factual record on which Hologic intends to rely to prove infringement at trial. To the extent that further discovery shows any element of an asserted claim is not present literally, Hologic will rely on the identified evidence to show that the element is present under the doctrine of equivalents.

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	<p>HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad Multi-Lumen Balloon Source Applicator for Brachytherapy is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.” Ref. No. 2 at 2232.</p> <p>“SenoRx, Inc. (NASDAQ:SENO) today announced that it has launched Contura™, its Multi-Lumen Balloon (MLB) Catheter for delivering brachytherapy to the surgical margins following lumpectomy for breast cancer.” Ref. No. 5.</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref.</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹						
	<p>No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p>						
<p>an expandable outer surface defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;</p>	<p><u>CONTENTION:</u></p> <p>The outer surface of the inflatable spherical Contura™ multi-lumen balloon (an “expandable surface element”) defines the three-dimensional apparatus volume that fills the interstitial void of the resection cavity. The expanded balloon conforms the cavity to the balloon shape and thereby defines the inner boundary of target tissue along the cavity wall that is being treated. This claim element is thus <u>literally</u> infringed.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen. The balloon is inflated to a 4 or 5 cm spherical shape by a controlled volume injection of physiological saline to approximately 32 or 55 ml, respectively.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator consists of a multi-lumen catheter attached to an inflatable spherical balloon (figure 1).” Ref. No. 2 at 2232.</p> <p>“The applicator is not intended for use in cavities that are too small, too large and/or of shapes unable to conform to an approximately spherical, 4 to 5 cm diameter SenoRx balloon.” Ref. No. 2 at 2232.</p> <p>“8. Using the syringes provided, inflate the Applicator balloon with the contrast media solution to the desired fill volume.</p> <table data-bbox="1087 1263 1780 1356"> <tr> <td>Desired balloon diameter</td><td>Approximate balloon fill volume</td></tr> <tr> <td>4 cm</td><td>33 ml</td></tr> <tr> <td>5 cm</td><td>58 ml</td></tr> </table> <p>Ref. No. 2 at 2232.</p>	Desired balloon diameter	Approximate balloon fill volume	4 cm	33 ml	5 cm	58 ml
Desired balloon diameter	Approximate balloon fill volume						
4 cm	33 ml						
5 cm	58 ml						

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	<p>An illustration of the Contura™ applicator shows the three-dimensional apparatus volume defined by the expandable polyurethane balloon to be inflated in the resection cavity. Ref. No. 3.</p> <p>“It’s a balloon-based device. The balloon is implanted into the breast and it replaces the tissue that was removed by the surgeon. And the goal of the treatment is to treat the rind of the tissue surrounding the balloon. This animation provided to us by the makers of the device shows how it works. After the balloon is inserted into the breast, it is inflated and filled with a saline solution.” Ref. 4.</p> <p>See generally Ref. No. 4 (showing expansion of balloon with subsequent increase in the three-dimensional apparatus volume).</p> <p>“SenoRx has developed Contura™, a multi-lumen radiation balloon applicator for accelerated partial breast irradiation. The radiation balloon uses vacuum to remove excess fluid and to adhere closely to often irregularly shaped lumpectomy cavities in order to deliver precise radiation dosing through multiple seed lumens.” Ref. No. 6</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p>
<p>a radiation source disposed completely within the expandable outer surface and located so as to be spaced apart from the apparatus volume,</p>	<p><u>CONTENTION:</u></p> <p>Each radiation source (“radiation source wire”) is inserted through a radiation source lumen in the Contura into its respective central or curved treatment lumen. The five treatment lumens are located within the expandable outer surface of the balloon, and do not contact the expandable outer surface of the device, which defines the apparatus volume. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 1 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	<p>HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen. The balloon is inflated to a 4 or 5 cm spherical shape by a controlled volume injection of physiological saline to approximately 32 or 55 ml, respectively.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator consists of a multi-lumen catheter attached to an inflatable spherical balloon (figure 1). Lumens are provided for attachment to commercially available HDR (High Dose Rate) remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen.” Ref. No. 2 at page 2232.</p> <p>“It’s a balloon-based device. The balloon is implanted into the breast and it replaces the tissue that was removed by the surgeon. And the goal of the treatment is to treat the rind of the tissue surrounding the balloon. This animation provided to us by the makers of the device shows how it works. After the balloon is inserted into the breast, it is inflated and filled with a saline solution. Then radioactive seeds are sent through five separate channels inside the balloon. The dose is actually directed by where the</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	<p>seed sits within the balloon. So, having one offset from the center of the balloon allows us to pull that dose by leaving the seed in the balloon for a certain period of time – longer than the other side has it for an example. And that means the dosage of the radiation is concentrated on the tumor and doesn't burn the patient's skin. And if the skin was too close to channel 1, we might put the seed longer in channel 3 and 4 versus channel 1 to cool down that side of the dose." Ref. 4.</p> <p>"In addition, the Contura MLB uses vacuum suction to remove excess seroma and air to enhance conformance of often irregularly shaped lumpectomy cavity walls to the balloon surface in order to deliver precise radiation dosing through multiple radiation source lumens." Ref. No. 5.</p> <p>An illustration of the Contura™ applicator shows the five treatment lumens (into which the radiation sources are inserted) located within the center of the expandable outer surface of the balloon. Ex. C. Ref. No. 3.</p> <p>"The Applicator red-capped radiation source wire lumens are numbered '1', '2', '3', '4' and '5' and positioned as shown in Figure 3. Lumen number '1' corresponds to the offset lumen closest and parallel to the longitudinal radiopaque line (M) along the outside of the catheter. Lumen number '5' corresponds to the central lumen. Remove the red caps and use commercially available connectors to attach the source lumens to the afterloader." Ref. No. 2 at 2232.</p> <p>See generally Ref. No. 4 (showing animated depiction of, and describing insertion of the radioactive seeds into the treatment lumens).</p> <p>See <i>also</i> evidence attached to Plaintiffs' Motion For Preliminary Injunction, Plaintiffs' Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte's Order Denying Plaintiffs' Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35 ; Ref. No. 36 ; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38 ; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.
the radiation source further being asymmetrically located and arranged within the expandable surface to provide predetermined asymmetric isodose curves with respect to the apparatus volume.	<p><u>CONTENTION:</u></p> <p>Each radiation source (“radiation source wire”) is inserted through a radiation source lumen into its respective central or curved treatment lumen. All of the treatment lumens are spaced apart from the apparatus volume (e.g., not touching the interior surface of the balloon), and are arranged asymmetrically with respect to the longitudinal axis of the catheter by the treating physician so as to irradiate the desired target tissue. The isodose surfaces or curves that are generated by the accused device will have a predetermined asymmetry with respect to the balloon. One way in which this asymmetric dosing is achieved is by varying the duration of time radioactive seeds reside within select treatment lumens. Commercially available treatment planning software is used by the physician to determine the appropriate parameters of the dosing for optimized radiation delivery of a prescribed dose to the targeted treatment volume. The optimized radiation delivery is reflected in asymmetric isodose curves. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 1 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	<p>HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen. The balloon is inflated to a 4 or 5 cm spherical shape by a controlled volume injection of physiological saline to approximately 32 or 55 ml, respectively.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator consists of a multi-lumen catheter attached to an inflatable spherical balloon (figure 1). Lumens are provided for attachment to commercially available HDR (High Dose Rate) remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen.” Ref. No. 2 at page 2232.</p> <p>“RADIATION DELIVERY - Refer to Figure 3</p> <p>1. CT imaging should be used in conjunction with commercially available treatment planning software to determine the appropriate source lumens, source dwell positions and dwell times for optimized radiation delivery of a prescribed dose to the targeted treatment volume.” Ref. No. 2 at 2232.</p> <p>“In addition, the Contura MLB uses vacuum suction to remove excess seroma and air to enhance conformance of often irregularly shaped lumpectomy cavity walls to the balloon surface in order to deliver precise radiation dosing through multiple radiation source lumens.” Ref. No. 5.</p> <p>An illustration of the Contura™ applicator shows the five treatment lumens, the outer spatial volume as defined by the expandable polyurethane balloon, and the inner spatial volume. Ref. No. 3.</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	<p>“The Applicator red-capped radiation source wire lumens are numbered ‘1’, ‘2’, ‘3’, ‘4’ and ‘5’ and positioned as shown in Figure 3. Lumen number ‘1’ corresponds to the offset lumen closest and parallel to the longitudinal radiopaque line (M) along the outside of the catheter. Lumen number ‘5’ corresponds to the central lumen. Remove the red caps and use commercially available connectors to attach the source lumens to the afterloader.” Ref. No. 2 at 2232.</p> <p>“It’s a balloon-based device. The balloon is implanted into the breast and it replaces the tissue that was removed by the surgeon. And the goal of the treatment is to treat the rind of the tissue surrounding the balloon. This animation provided to us by the makers of the device shows how it works. After the balloon is inserted into the breast, it is inflated and filled with a saline solution. Then radioactive seeds are sent through five separate channels inside the balloon. The dose is actually directed by where the seed sits within the balloon. So, having one offset from the center of the balloon allows us to pull that dose by leaving the seed in the balloon for a certain period of time – longer than the other side has it for an example. And that means the dosage of the radiation is concentrated on the tumor and doesn’t burn the patient’s skin. And if the skin was too close to channel 1, we might put the seed longer in channel 3 and 4 versus channel 1 to cool down that side of the dose.” Ref. 4.</p> <p>See generally Ref. No. 4 (describing insertion of the radioactive seeds into the treatment lumens, showing animated depiction of the asymmetric treatment achieved by insertion of radioactive seeds into a select treatment lumen, and showing animated depiction of asymmetric isodose curves).</p> <p>See also evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See also Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35 ; Ref. No. 36 ; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38 ; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.
6. A surgical apparatus for providing radiation treatment to target tissue comprising:	<p><u>CONTENTION:</u></p> <p>The SenoRad Multi-Lumen Balloon Source Applicator (“Contura™”) is an interstitial brachytherapy apparatus designed to deliver localized radiation to the margins of the cavity remaining after surgical resection of breast cancer.</p> <p>SenoRx Inc. (“SenoRx”) makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 6 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	<p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad Multi-Lumen Balloon Source Applicator for Brachytherapy is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.” Ref. No. 2 at 2232.</p> <p>“SenoRx, Inc. (NASDAQ:SENO) today announced that it has launched Contura™, its Multi-Lumen Balloon (MLB) Catheter for delivering brachytherapy to the surgical margins following lumpectomy for breast cancer.” Ref. No. 5.</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹						
	HOL00002016-2019, 2030.						
an expandable outer surface defining an apparatus volume;	<p><u>CONTENTION:</u></p> <p>The outer surface of the inflatable spherical Contura™ multi-lumen balloon is an expandable surface element, and defines the three-dimensional apparatus volume that fills the resection cavity. This claim element is thus <u>literally</u> infringed.</p> <p><u>SUPPORT:</u></p> <p>“The SenoRad applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen. The balloon is inflated to a 4 or 5 cm spherical shape by a controlled volume injection of physiological saline to approximately 32 or 55 ml, respectively.” Ref. No. 1 at Device description.</p> <p>“The Contura™ MLB Applicator consists of a multi-lumen catheter attached to an inflatable spherical balloon (figure 1).” Ref. No. 2 at 2232.</p> <p>“The applicator is not intended for use in cavities that are too small, too large and/or of shapes unable to conform to an approximately spherical, 4 to 5 cm diameter SenoRx balloon.” Ref. No. 2 at 2232.</p> <p>“8. Using the syringes provided, inflate the Applicator balloon with the contrast media solution to the desired fill volume.</p> <table data-bbox="1087 1143 1780 1235"> <tr> <td>Desired balloon diameter</td><td>Approximate balloon fill volume</td></tr> <tr> <td>4 cm</td><td>33 ml</td></tr> <tr> <td>5 cm</td><td>58 ml</td></tr> </table> <p>Ref. No. 2 at 2232.</p> <p>An illustration of the Contura™ applicator shows the three-dimensional apparatus volume defined by the expandable polyurethane balloon to be inflated in the resection cavity. Ref. No. 3.</p>	Desired balloon diameter	Approximate balloon fill volume	4 cm	33 ml	5 cm	58 ml
Desired balloon diameter	Approximate balloon fill volume						
4 cm	33 ml						
5 cm	58 ml						

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	<p>“It’s a balloon-based device. The balloon is implanted into the breast and it replaces the tissue that was removed by the surgeon. And the goal of the treatment is to treat the rind of the tissue surrounding the balloon. This animation provided to us by the makers of the device shows how it works. After the balloon is inserted into the breast, it is inflated and filled with a saline solution.” Ref. 4.</p> <p>See generally Ref. No. 4 (showing expansion of balloon with subsequent increase in the three-dimensional apparatus volume).</p> <p>“SenoRx has developed Contura™, a multi-lumen radiation balloon applicator for accelerated partial breast irradiation. The radiation balloon uses vacuum to remove excess fluid and to adhere closely to often irregularly shaped lumpectomy cavities in order to deliver precise radiation dosing through multiple seed lumens.” Ref. No. 6</p> <p>See also evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p>
<p>a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of radiation sources being provided on at least two elongate members extending into the apparatus volume, at least one of the elongate members being shaped to provide asymmetric placement of a radiation source with respect to a longitudinal axis through the apparatus volume.</p>	<p><u>CONTENTION:</u></p> <p>The radiation source wires are inserted into the treatment lumens within the Contura balloon during treatment and removed after the desired fractional dose has been delivered, thereby satisfying the requirement of a radiation source that is “replaceably disposable within the expandable outer surface.” The multiple treatment lumens of the Contura allow multiple solid radiation sources (e.g., single radionuclide sources on multiple separate source wires) to be arrayed simultaneously within two or more separate treatment lumens so as to irradiate a select area of tissue with a dose that has predetermined asymmetric isodose curves. Alternatively, the multiple treatment lumens of the Contura allow one or more solid radiation sources to be arrayed at different points in time within one or more separate treatment lumens to provide an isodose profile having a shape substantially similar to the shape of the balloon within the targeted tissue. The offset treatment lumens are curved to provide asymmetric placement of the radiation source with respect to the central treatment lumen which traces the longitudinal axis through the treatment volume. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 1 by making, using, marketing, offering for sale, selling, supplying, and distributing the</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	<p>Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>“The radiation balloon uses vacuum to remove excess air and fluid and to adhere closely to often irregularly shaped lumpectomy cavities in order to deliver precise radiation dosing through multiple seed lumens.” Ref. No. 17 at SRX-HOL00006639.</p> <p>“Each lumen can accommodate 8 dwell positions.” Ref. No. 17 at SRX-HOL00006642.</p> <p>“8 dwell positions are available within each lumen. 5 lumens x 8 dwell positions=40 possible dwell positions for each patient!” Ref. No. 16 at SRX-HOL00006600</p> <p>See <i>also</i> evidence attached to Plaintiffs’ Motion For Preliminary Injunction, Plaintiffs’ Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte’s Order Denying Plaintiffs’ Motion For Preliminary Injunction.</p> <p>See <i>also</i> Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	<p>SRX-HOL00006734, 6780-3784; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p>
<p>8. The apparatus of claim 1, wherein the expandable outer surface is sufficiently rigid to deform the target tissue into the shape of the expandable outer surface, causing the predetermined asymmetric isodose curves to penetrate into the target tissue to a prescribed depth.</p>	<p><u>CONTENTION:</u></p> <p>The SenoRad Multi-Lumen Balloon Source Applicator (“Contura™”) is an interstitial brachytherapy apparatus designed to deliver localized radiation to the margins of the cavity remaining after surgical resection of breast cancer. The Contura™ is inserted into a cavity remaining after the excision of a breast tumor. Once the balloon is in the cavity, the balloon is inflated with a contrast media or saline (injected through the inflation port). The Contura balloon is sufficiently rigid to conform the cavity to the shape of the balloon. Parameters of the balloon size and location are adjusted to conform to the surgical margin of the tissue to the shape of the outer volume of the balloon. Once the resection cavity has been conformed to the shape of the expandable outer surface, insertion of radiation source wires into select treatment lumens for prescribed lengths of time controls the dose of radiation targeting the tissue, so as to irradiate a select area of tissue with a dose that has predetermined asymmetric isodose curves., thereby preventing damage to healthy tissue proximate to the surface of the balloon. This claim element is thus <u>literally</u> infringed.</p> <p>SenoRx Inc. (“SenoRx”) makes, uses, offers for sale, and sells an interstitial brachytherapy applicator marketed under the product name Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404; Ref. No. 25 at SRX-HOL00003386; Ref. No. 27; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 35; Ref. No. 36; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788; Ref. No.</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	<p>42 at SRX-HOL00002016-2019, 2030..</p> <p>SenoRx also induces and contributes to direct infringement by others of claim 8 by making, using, marketing, offering for sale, selling, supplying, and distributing the Contura™ to physicians and health care facilities for use in treating breast cancer patients. See Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 22; Ref. No. 26; Ref. No. 34 at SRX-HOL00006734, 6780-3784; Ref. No. 28 at SRX-HOL00004163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 37 at SRX-HOL00004778; Ref. No. 39 at SRX-HOL00001540; Ref. No. 41 at SRX-HOL00001792-1794; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 42 at SRX-HOL00002016-2019, 2030.</p> <p>SenoRx has made, used, marketed, offered for sale, sold, supplied, and distributed the Contura knowing that it is especially made or especially adapted for infringing use. Ref. No. 23 at SRX-HOL5408-5429; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55. The Contura is not a staple article or commodity of commerce suitable for substantial non-infringing use.</p> <p><u>SUPPORT:</u></p> <p>See also evidence attached to Plaintiffs' Motion For Preliminary Injunction, Plaintiffs' Reply Brief In Support of Motion For Preliminary Injunction, and evidence cited in Judge Whyte's Order Denying Plaintiffs' Motion For Preliminary Injunction.</p> <p>See also Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429.</p> <p>See also Ref. No. 7; Ref. No. 8; Ref. No. 10 at SRX-HOL00002354; Ref. No. 11 at SRX-HOL00002360-2362; Ref. No. 12 at 1, 2; Ref. No. 13 at 39; Ref. No. 14 at SRX-HOL00002371, 2373; Ref. No. 15 at SRX-HOL00007179-7186; Ref. No. 16 at SRX-HOL00006591-6601; Ref. No. 17; Ref. No. 23 at SRX-HOL00005396, 5404, 5408-5429; Ref. No. 22; Ref. No. 25 at SRX-HOL00003386; Ref. No. 26; Ref. No. 34 at</p>

Asserted Claim	Contura™ Multi-Lumen Balloon Source Applicator ¹
	SRX-HOL00006734, 6780-3784; Ref. No. 27 ; Ref. No. 28 at SRX-HOL00004140-4149, 4163-4195; Ref. No. 29 at SRX-HOL00004197-4215; Ref. No. 30 ; Ref. No. 31 at HOLOGIC0048742; Ref. No. 32 at HOLOGIC0048754-55; Ref. No. 33 at SRX-HOL00004457-4459; Ref. No. 34 at SRX-HOL00006734, 6740, 6743-6745, 6760-6773, 6780-3784; Ref. No. 35 ; Ref. No. 36 ; Ref. No. 37 at SRX-HOL00004778; Ref. No. 38 ; Ref. No. 39 at SRX-HOL00001540; Ref. No. 40 at SRX-HOL00001675-1688, 1692-1702; Ref. No. 41 at SRX-HOL00001784-1788, 1792-1794; Ref. No. 42 at SRX-HOL00002016-2019, 2030.

Appendix D

APPENDIX D
Materials Relied Upon and Cited Within the Infringement Charts

Ref. No.	Document Description
1	SenoRx's 510(k) Summary for SenoRad Multi-Lumen Balloon Source Applicator for Brachytherapy [SRX-HOL0000 6605-6606]
2	Contura™ Multi-Lumen Balloon Source Applicator for Brachytherapy- Instructions for Use [SRX-HOL00002232-2233]
3	Contura brochure, posted at http://www.senorx.com/images/SNRX_7000_conturads_7.jpg [SRX-HOL00003402]
4	Contura™ Balloon Applicator Insertion Procedure and Radiation Procedure Animation, posted at http://www.myfoxphoenix.com/myfox/pages/Home/Detail.jsessionid=18E5571CEC66E18169DF1494828ED0A5?contentId=5126377&version=1&locale=EN-US&layoutCode=VSTY&pageId=1.1.1&sflg=1
5	SenoRx press release, January 17, 2008, posted at http://www.senorx.com/siteadmin/files/SenoRxLaunchesContura.pdf
6	SenoRx webpage discussing Contura™, posted at http://www.senorx.com/teatment.asp [HOLOGIC0048885-48887]
7	Gearhart Email re conference call with Contura Targets.xls attachment [SRX-HOL00006882-6898]
8	Sales spreadsheet [SRX-HOL00003362-3379]
9	Contura Multi-Lumen Balloon: Product Overview and Dosimetry [SRX-HOL00006487-6497]
10	Canaccord Adams Flash Update 19 February 2008 [SRX-HOL00002354-2358]
11	Canaccord Adams Flash Update 20 February 2008 [SRX-HOL00002360-2370]
12	Press Release: "SenoRx Reports Revenue Growth of 43.2 Percent in Q4 2007 Compared with Q4 2006" (Ex-99.1 to SenoRx 8-K, filed February 19, 2008), posted at http://www.sec.gov/Archives/edgar/data/1097136/000119312508033236/dex991.htm
13	SenoRx 10-K for fiscal year ending December 31, 2007, posted at http://www.sec.gov/Archives/edgar/data/1097136/000119312508062802/d10k.htm [HOLOGIC0048793-48884]
14	CitiGroup Global Markets February 19, 2008 Company Focus: SenoRx, Inc. [SRX-HOL00002371-2379]
15	2008 Contura Market Plan, dated December 20 th , 2007 [SRX-HOL00007170-7187]
16	SenoRx document "How to set up an account for Contura [SRX-HOL00006591-6611]
17	SenoRx sales training manual [SRX-HOL00006616-6686]

18	SenoRx sales invoices, returned goods authorizations, shipping requests, sales orders, price list, ordering information, and related materials [SRX-HOL00000523-1503]
19	Contura MLB Source Applicator For Brachytherapy-Special 510(K) [SRX-HOL00005564-5565]
20	Risk Analysis Report: Contura MLB Brachytherapy Applicator [SRX-HOL00004119-4128]
21	Technical Drawings- [SRX-HOL00004861-4863, 4877-4878, 4933-4934]
22	Exhibit G to Plaintiffs' Amended Complaint [HOLOGIC0048776-48792]
23	MammoSite Instructions For Use [SRX-HOL00005396-5429]
24	April 27, 2007 Claim Construction Order for <i>Xoft</i> litigation (Case NO. C-05-05312 RMW)
25	SenoRx Fourth Quarter/FY 2007 Conference call [SRX-HOL00003380-3397]
26	Multi-Site Prospective, Non-Randomized Study Utilizing The Contura™ Multi-Lumen Balloon (MLB) Breast Brachytherapy Applicator To Deliver Accelerated Partial Breast Irradiation: Analysis of Dosimetric Success, Local Tumor Control, Cosmetic Outcome, Acute and Chronic Toxicity, and Clinical Scenarios For Optimal Use [SRX-HOL00003312-3361]
27	Design History File Checklist [SRX-HOL00004092-4093]
28	Dosimetric Comparative Analysis of MammoSite and SenoRx catheters [SRX-HOL00004140-4195]
29	Comparison between MammoSite and SenoRx when using the offset Catheters [SRX-HOL00004197-4215]
30	Radiation Balloon Dosimetry Measurement [SRX-HOL00004237-4455]
31	U.S. Patent No. 6,923,754 (Lubbock) [HOLOGIC0048742-48753]
32	U.S. Patent No. 6,955,641 (Lubbock) [HOLOGIC0048754-48775]
33	Tests for Compliance of the SenoRx balloon catheter device with the Varian Varisource and GammaMed afterloaders [SRX-HOL4457-4460]
34	Contura Multi-Lumen Balloon: Expanding your Treatment Possibilities [SRX-HOL00006733-6786]
35	SenoRx Radiation Balloon Product Specification [SRX-HOL00004601-4603]
36	Communication Dorin Todor to Paul Lubbock [SRX-HOL00004231-4235]
37	Contura Multi-Lumen Balloon-Expanding Your Treatment Possibilities [SRX-HOL00004776-4778]
38	Contura 4-5 Cm Inflation Volume vs. Balloon Diameter {XRS-HOL00003738-3746}
39	SenoRx Inc. Board of Directors' Meeting June 14, 2007 [SRX-HOL00001504-1664]

40	SenoRx Inc. Board of Directors' Meeting September 26, 2007 [SRX-HOL00001665-1774]
41	SenoRx Inc. Board of Directors' Meeting December 2, 2007 [SRX-HOL00001775-1954]
42	SenoRx Inc. Board of Directors' Meeting February 27, 2008 [SRX-HOL00001955-2048]

Exhibit 12



COPY OF PAPERS
ORIGINALLY FILED

Docket No.: 101360-16
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Rance A. Winkler, et al.


Application No.: 09/464,727-7988

Group Art Unit: 3736

Filed: December 16, 1999

Examiner: J. Lacyk

For: ASYMMETRIC RADIATION DOSING
APPARATUS AND METHOD

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on the date shown below.
Dated: 2/27/02 Signature: 
(Ronald E. Cahill)

AMENDMENT

Commissioner for Patents
Washington, DC 20231

Dear Sir:

In response to the Office Action dated October 31, 2001 (Paper No. 5), please amend the above-identified U.S. patent application by replacing all of the claims with the Clean Copy of All Pending Claims below. A Complete Set of Pending Claims With Markings to Show Amendments Made is attached to this Amendment following the signature page.

03/14/2002 55174181 00000039 99464727

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03/14/2002 55174181 00000039 99464727

02 FC:202

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Application No.: 09/464,727-7988

Docket No.: 101360-16

Clean Copy of All Pending Claims

1. (Amended) An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:

an expandable outer surface defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

a radiation source disposed completely within the expandable outer surface and located so as to be spaced apart from the apparatus volume, the radiation source further being asymmetrically located and arranged within the expandable surface to provide predetermined asymmetric isodose curves with respect to the apparatus volume.

2. (Amended) A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

A | a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of solid radiation sources being provided in a spaced apart relationship on a single elongate member, the single elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources with respect to a longitudinal axis through the apparatus volume.

3. The apparatus of claim 2, further comprising a catheter in communication with the apparatus volume, the elongate member extending through the catheter into the apparatus volume.

4. The apparatus of claim 3, wherein the elongate member is formed of a shape memory alloy, the elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources, taking on a substantially straight shape while being inserted through the catheter to the apparatus volume, and resuming an asymmetric shape when extended into the apparatus volume.

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5. (Amended) A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, wherein at least one of the plurality of solid radiation sources has a different specific activity from at least one other solid radiation source.

6. (Amended) A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

AI a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of radiation sources being provided on at least two elongate members extending into the apparatus volume, at least one of the elongate members being shaped to provide asymmetric placement of a radiation source with respect to a longitudinal axis through the apparatus volume.

7. The apparatus of claim 6, wherein each of the at least two elongate members includes a plurality of solid radiation sources provided in a spaced apart relationship.

8. The apparatus of claim 1, wherein the expandable outer surface is sufficiently rigid to deform the target tissue into the shape of the expandable outer surface, causing the predetermined asymmetric isodose curves to penetrate into the target tissue to a prescribed depth.

9. (Amended) An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:

an expandable outer surface having a base and defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

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a radiation source disposed completely within and spaced apart from the expandable outer surface; and

an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves with respect to the apparatus volume.

10. (Amended) The apparatus of claim 9, wherein the asymmetric radiation shield comprises a radio-opaque material disposed on only a portion of the expandable outer surface.

11. The apparatus of claim 10, wherein the expandable outer surface comprises an inflatable balloon.

12. The apparatus of claim 11, wherein the radiation shield comprises a barium material disposed a portion of the inflatable balloon.

13. The apparatus of claim 9, further comprising at least one radiation shield extending from the base of the expandable outer surface toward an opposite end of the expandable surface, the shield being in between and spaced apart from the radiation source and the expandable outer surface, the shield forming a radio-opaque barrier between a portion of the radiation source and the target tissue.

14. The apparatus of claim 13, wherein the radiation shield comprises two shields provided on opposite sides of the radiation source.

15. Canceled.

16. Canceled.

17. Canceled.

18. Canceled.

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19. Canceled.

Application No.: 09/464,727-7988

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REMARKS/ARGUMENTS

Applicants appreciate the Examiner's indication that claims 2 through 7 define allowable subject matter. Applicants have amended claims 2, 5 and 6 to be independent claims including the recitations of the base claim and any intervening claims and to correct any rejections under 35 U.S.C. § 112, second paragraph. Applicants have also amended the preamble to read that the recited apparatus is a surgical apparatus for providing radiation treatment to target tissue. This amendment is supported in the opening paragraph of the Detailed Description of the Invention.

Applicants have amended independent claim 1 (from which claim 8 depends) and independent claim 9 (from which claims 10 to 14 depend, directly or ultimately) to better define the invention. Applicants have also amended claim 10 to recite that radio-opaque material is disposed *only* on a portion of the expandable surface. Applicants cancel claims 15 to 19 herein. Accordingly, claims 1 to 14 are now pending.

Claim Rejections Over McGrath

Claims 1 and 9 stand rejected as anticipated by McGrath (US 6,036,631) under 35 U.S.C. § 102(e). In particular, the Examiner states that "McGrath et al discloses a device for treating tissue having an expandable outer surface and a radiation source disposed within the expandable surface having a plurality of solid radiation sources (Fig. 2B). McGrath et al also teaches the use of shielding to absorb some of the radiation."

McGrath is directed to a device and method for treatment of cancerous tissue from a body conduit, i.e., interluminal treatment. By contrast, Applicants' apparatus is an interstitial brachytherapy apparatus, used to treat remaining proliferative tissue surrounding a surgical extraction site such as might be found in the treatment of brain or breast cancers. As a result of this difference in purpose, there are a number of key differences in structure between McGrath and claims 1 and 9.

For example, the expandable outer surface of claims 1 and 9 defines a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated. (See Page 7, lines 8 to 15.) Further, the radiation source is disposed completely within the expandable surface and is spaced apart from the apparatus volume. (See Page 8, line 23 to page 9 line 13, noting the

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advantages of providing the radiation source within the interstitial volume and spaced apart from the target tissue; See also each of FIGS. 1 and 3 through 9, showing the radiation sources disposed entirely within the expandable surface). Further with respect to claim 1, the radiation source is located and arranged within the expandable outer surface so as to create asymmetric radiation isodose curves with respect to the apparatus volume. (See Page 9, line 23 to page 10, line 7.) That is, the radiation source is arranged within the device so that asymmetric dosing appears at the apparatus volume, which is configured to correspond to the interstitial void created by surgical extraction of diseased tissue.

The device of McGrath is not configured for use interstitially, it is configured for use interluminally, with balloons provided only to hold its catheter within a lumen, or to dilate the lumen. Accordingly, the radiation source in McGrath is not located completely within any of the disclosed balloons, nor is it located and arranged to provide an asymmetric dose at an apparatus volume that conforms to an interstitial void. Rather, McGrath provides an x-ray tube 48 that slides within a catheter, or a plurality of radiation-emitting seeds 52 "essentially forming a linear source." (Column 5, lines 34 to 37.) Accordingly, McGrath lacks several of the features recited in claim 1.

McGrath also lacks the features recited in claim 8 which depends from claim 1. Claim 8 recites that the expandable outer surface is sufficiently rigid to deform the target tissue into the shape of the expandable outer surface, causing the predetermined asymmetric isodose curves to penetrate into the target tissue to a prescribed depth. That is, the expandable outer surface actually causes the interstitial void to take on the same shape as the apparatus volume so that, even for oddly shaped voids in soft tissue, the shape of the target tissue that is to receive the asymmetric radiation dose will be the same as for the apparatus volume, enabling precise delivery of prescription doses of radiation asymmetrically from Applicants' claimed configuration.

As described above, McGrath does not disclose, teach or suggest the configuration that is recited in claim 9 that is also recited in claim 1. In addition to the structure it recites in common with claim 1, claim 9 recites an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves with

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respect to the apparatus volume. No portion of McGrath provides an outer expandable surface defining such an apparatus volume, and, while other configurations are referred to generically, the shielding that is provided by McGrath is simply a tubular shield that protects the bladder neck and sphincter. (See, Column 10, lines 7 to 39.) Nowhere does McGrath disclose, teach or suggest providing asymmetric shielding spaced apart from a radiation source so as to create predetermined asymmetric isodose curves with respect to an apparatus volume defined by the outer expandable surface.

Claim Rejections Over Ciezki in view of Apple

Claims 1 and 8 to 14 stand rejected as unpatentable over Ciezki (EP 0 867 200) in view of Apple (WO 99/33515) under 35 U.S.C. § 103. In particular, the Examiner states that:

Ciezki et al teaches a treatment device having a plurality of radiation sources disposed in a catheter. Ciezki et al also teaches the use of shielding or an attenuator made from a radio-opaque material i.e. tantalum. Ciezki et al teaches the claimed device except for the use of an inflatable balloon catheter or the specific use of barium as the shielding material. Apple et al teaches a radioactive treatment device that uses an inflatable balloon to place the catheter at the treatment site. . . . Therefore a modification of Ciezki et al such that the catheter includes an inflatable balloon would have been obvious to help in the placement and retention of the catheter at the treatment site;

The combination of Ciezki and Apple suffers from all of the same problems as McGrath docs. Regarding claim 1, the Examiner recognizes that Ciezki does not provide an expandable outer surface defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated; and a radiation source disposed completely within the expandable outer surface and located so as to be spaced apart from the apparatus volume. Apple does not fill in this missing teaching. Apple is directed to a catheter apparatus that is filled with a radioactive gas. The catheter can be used to treat restenosis after angioplasty, or it can treat malignancies. The "restenosis" configuration includes a number of balloons of the type generally used to hold a catheter in an artery; that is, interlumenally. None of these balloons define an apparatus volume within an interstitial void within which the radioactive source is completely placed. Even where Apple discloses a device for interstitial use (See, e.g., FIGS. 17 to 19), the radiation source completely fills the balloon and is not in a spaced apart relationship from the balloon as is recited in claim 1. Thus, even if a balloon from Apple was added to Ciezki, the configuration of claim

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I would not result.

More significantly, neither Apple nor Ciezki nor their combination teaches asymmetric placement of a radiation source that is completely within an expandable surface defining an apparatus volume so as to result in asymmetric radiation isodose curves with respect to the apparatus volume. As described above and in the portions of the application cited above, Applicants' configuration provides significant advantages in the treatment of marginal proliferative tissue surrounding an interstitial void left by a surgical tumor resection. Accordingly, neither Ciezki nor Apple nor their combination renders the subject matter of claim 1 unpatentable to Applicants. Claim 8, which depends from claim 1, is further patentable over Ciezki and Apple because neither teaches or suggests the recitations of claim 8 for the same reasons as described above with respect to McGrath.

As described above, neither Ciezki nor Apple nor their combination discloses, teaches or suggests the configuration that is recited in claim 9 that is also recited in claim 1 – that is, an expandable outer surface having a base and defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated; and a radiation source disposed completely within and spaced apart from the expandable outer surface.

In addition to the structure it recites in common with claim 1, claim 9 recites an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves with respect to the apparatus volume. No portion of Ciezki defines such an apparatus volume and the only embodiment of Apple that provides an apparatus volume (FIGS 17 to 19) does not include any shielding. Where Ciezki and Apple do provide shielding, it is to protect blood flowing through the apparatus as it irradiates an arterial wall. The disclosed shielding does not provide asymmetric radiation dosing with respect to an expandable outer surface defining an apparatus volume, because there is no such volume in these references. As described above and in the portions of the application cited above, Applicants' configuration with asymmetric shielding provides significant advantages in that it provides precise delivery of prescription doses of radiation asymmetrically about an interstitial void created by surgical resection of diseased tissue. Neither of these references, alone or

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combined, teach or suggest a device that achieves this result.

Conclusion

For all of the foregoing reasons, Applicants request that the Examiner reconsider the application and allow each of claims 1 to 14 to issue. If the Examiner believes that an interview would facilitate the resolution of any outstanding issues, the Examiner is kindly requested to contact the undersigned.

Dated: 2/27/02

Respectfully submitted,

By 

Ronald E. Cahill

Registration No.: 38,403

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Application No.: 09/464,727-7988

Docket No.: 101360-16

Complete Set of Pending Claims With Markings to Show Amendments Made

1. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:

an expandable outer surface defining [an] a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

a radiation source [replaceably disposable] disposed completely within the expandable outer surface and located so as to be spaced apart from the apparatus volume, the radiation source [comprising a plurality of solid radiation sources arranged] further being asymmetrically located and arranged within the expandable surface to provide predetermined asymmetric isodose curves [within the target tissue] with respect to the apparatus volume,

2. [The apparatus of claim 1, wherein a] A surgical apparatus for providing radiation treatment to target tissue comprising;

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of solid radiation sources [are] being provided in a spaced apart relationship on a single elongate member, the single elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources with respect to a longitudinal axis through the apparatus volume.

3. The apparatus of claim 2, further comprising a catheter in communication with the apparatus volume, the elongate member extending through the catheter into the apparatus volume.

4. The apparatus of claim 3, wherein the elongate member is formed of a shape memory alloy, the elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources, taking on a substantially straight shape while being inserted through the

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catheter to the apparatus volume, and resuming an asymmetric shape when extended into the apparatus volume.

5. [The apparatus of claim 1,] A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, wherein at least one of the plurality of solid radiation sources has a different specific activity from at least one other solid radiation source.

6. [The apparatus of claim 1, wherein] A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of radiation sources [are] being provided on at least two elongate members extending into the apparatus volume, at least one of the elongate members being shaped to provide asymmetric placement of a radiation source with respect to a longitudinal axis through the apparatus volume.

7. The apparatus of claim 6, wherein each of the at least two elongate members includes a plurality of solid radiation sources provided in a spaced apart relationship.

8. The apparatus of claim 1, wherein the expandable outer surface is sufficiently rigid to deform the target tissue into the shape of the expandable outer surface, causing the predetermined asymmetric isodose curves to penetrate into the target tissue to a prescribed depth.

9. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:

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an expandable outer surface having a base and defining [an] a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

a radiation source [replaceably disposable] disposed completely within and spaced apart from the expandable outer surface; and

an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves [within the target tissue] with respect to the apparatus volume.

10. The apparatus of claim 9, wherein the asymmetric radiation shield comprises a radio-opaque material disposed on only a portion of the expandable outer surface.
 11. The apparatus of claim 10, wherein the expandable outer surface comprises an inflatable balloon.
 12. The apparatus of claim 11, wherein the radiation shield comprises a barium material disposed a portion of the inflatable balloon.
 13. The apparatus of claim 9, further comprising at least one radiation shield extending from the base of the expandable outer surface toward an opposite end of the expandable surface, the shield being in between and spaced apart from the radiation source and the expandable outer surface, the shield forming a radio-opaque barrier between a portion of the radiation source and the target tissue.
 14. The apparatus of claim 13, wherein the radiation shield comprises two shields provided on opposite sides of the radiation source.
 15. Canceled.
 16. Canceled.
 17. Canceled.
 18. Canceled.
- B

Application No.: 09/464,727-7988

Docket No.: 101360-16

19. Canceled.

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Exhibit 13

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Attorneys for Plaintiffs

HOLOGIC, INC., CYTYC CORPORATION and HOLOGIC L.P.

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

HOLOGIC, INC., CYTYC CORPORATION,
and HOLOGIC L.P.,

Plaintiffs,

vs.

SENORX, INC.,

Defendant.

AND RELATED COUNTERCLAIMS.

Case No. C08 00133 RMW (RS)

**PLAINTIFFS' PRELIMINARY CLAIM
CONSTRUCTION, AND IDENTIFICATION
OF STRUCTURE CORRESPONDING TO §
112(6) ELEMENTS FOR U.S. PATENT NOS.
5,913,813, 6,413,204, AND 6,482,142, AND
PRELIMINARY IDENTIFICATION OF
EVIDENCE PURSUANT TO PATENT
LOCAL RULE 4-2**

1 Pursuant to the parties' Proposed Stipulated Scheduling Order and Patent Local Rule 4-2(a) and
2 (b), Plaintiffs' Hologic, Inc, Cytac Corporation, and Hologic L.P. (collectively, "Hologic") hereby
3 provide their Preliminary Claim Construction, Identification of Structure

4 Corresponding to § 112(6) Elements, and Preliminary Identification of Extrinsic and Intrinsic
5 Evidence for certain terms, phrases and clauses in the asserted claims of U.S. Patent Nos. 5,913,813
6 (the "'813 patent"), 6,413,204 (the "'204 patent"), and 6,482,142 (the "'142 patent"), attached hereto
7 at Exhibits A, B, and C, respectively.

8 The claim constructions proposed in Exhibits A, B, and C are preliminary in nature, and
9 Hologic reserves the right to modify, amend, alter, and/or supplement these proposed claim
10 constructions. Hologic further reserves the right to modify and/or supplement the intrinsic and
11 extrinsic evidence cited in support of its proposed claim constructions including, without limitation,
12 the identification of supporting expert testimony. Hologic will provide a final statement of whether it
13 intends to present expert testimony and a summary of such testimony in accordance with Patent Local
14 Rule 4-3 and the schedule set forth in the parties' agreed Scheduling Order.

15 Hologic believes that any additional claim terms, phrases and clauses that SenoRx, Inc.
16 ("SenoRx") identified as requiring construction should be accorded their plain and ordinary meaning
17 and do not require construction by the Court. Hologic reserves the right, however, to offer its own
18 proposed constructions of any such additional claim terms, phrases and clauses upon review of and in
19 response to SenoRx's proposed claim constructions, and as part of the parties' meet and confer process
20 under Patent Local Rule 4-2(c).

21 Nothing in the proposed constructions in Exhibits A, B, and C is intended as an admission that
22 any claim term, phrase or clause has a particular meaning in the asserted claims of the '813, '204,
23 and/or '142 patents. Hologic expressly reserves the right to amend its contentions with respect to the

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1 meaning of any claim term or phrase as the parties meet and confer pursuant to Patent Local Rule 4-2(c)
2 or as discovery proceeds.

3 Dated: May 12, 2008

HOWREY LLP

5
6 By: Katharine L. Altemus
Katharine L. Altemus

8 HOWREY LLP
9 Attorneys for Plaintiffs
10 Hologic, Inc., Cytoc Corporation,
11 and Hologic L.P.
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PROOF OF SERVICE

I am employed in the County of San Mateo, State of California. I am over the age of 18 and not a party to the within action. My business address is 1950 University Avenue, 4th Floor, East Palo Alto, California 94303.

On May 12, 2008, I served on the interested parties in said action the within:

**PLAINTIFFS' PRELIMINARY CLAIM CONSTRUCTION, AND IDENTIFICATION OF
STRUCTURE CORRESPONDING TO § 112(6) ELEMENTS FOR U.S. PATENT NOS.
5,913,813, 6,413,204, AND 6,482,142, AND PRELIMINARY IDENTIFICATION OF
EVIDENCE PURSUANT TO PATENT LOCAL RULE 4-2**

by placing a true copy thereof in a sealed envelope(s) addressed as stated below and causing such envelope(s) to be deposited in the U.S. Mail at East Palo Alto, California.

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☒ (MAIL) I am readily familiar with this firm's practice of collection and processing correspondence for mailing. Under that practice it would be deposited with the U.S. postal service on that same day in the ordinary course of business. I am aware that on motion of party served, service is presumed invalid if postal cancellation date or postage meter date is more than 1 day after date of deposit for mailing in affidavit.

☒ (EMAIL/ELECTRONIC TRANSMISSION) Based on a court order or an agreement of the parties to accept service by e-mail or electronic transmission, I caused the documents to be sent to the persons at the e-mail addresses listed above. I did not receive, within a reasonable time after the submission, any electronic message or other indication that the transmission was unsuccessful.

I declare under penalty of perjury that I am employed in the office of a member of the bar of this Court at whose direction the service was made and that the foregoing is true and correct.

Executed on May 12, 2008, at East Palo Alto, California.

Sonya Schwab
(Type or print name)



(Signature)

Exhibit A

EXHIBIT A
U.S. Patent No. 5,913,813

'813 CLAIM TERM AT ISSUE	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
"inner spatial volume" (claims 1, 2, 12)	<i>a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide</i>	Abstract Col. 1:50 – col. 2:3 Col. 2:33-38, 44-63 Col. 3:9-16, 42-48 Col. 3:64 – col. 4:12 Col. 4:16-20, 21-31, 32-52 Figs. 1, 3-5 Notice of allowability (12-18-98) at 2 September 8, 1998 Amendment at 3-7 4-27-07 Claim Construction Order at 3-5, 28 (Case No. C-05-05312 RMW), and all evidence of record relating to the claim construction proceeding in that case 4-25-08 Order Denying Plaintiffs' Motion For Preliminary Injunction at 6-8

'813 CLAIM TERM AT ISSUE	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
"outer, closed, inflatable, chamber" (claim 1)	<i>outer, closed, inflatable chamber</i>	Abstract Col. 1:26 - 46 Col. 2:37-41 Col. 4:21-31, 40-45 Figs. 1, 3-5 Notice of allowability (12-18-98) at 2 September 8, 1998 Amendment at 3-7 4-27-07 Claim Construction Order at 6, 28 (Case No. C-05-05312 RMW)), and all evidence of record relating to the claim construction proceeding in that case
"predetermined constant spacing between said inner spatial volume and the radiation transparent wall" (claim 1)	<i>spacing predetermined by one skilled in the art between the wall or edge of the inner spatial volume and the radiation transparent wall of the outer, closed, inflatable chamber, when inflated, which is constant in all directions if the outer chamber is spherical, or constant along a radial plane if the outer chamber is not spherical</i>	Abstract Col. 1:26 – 46 Col 3:10-13 Col 4:13-20 Col. 4:21-31 Notice of allowability (12-18-98) at 2 September 8, 1998 Amendment at 3-7 4-27-07 Claim Construction Order at 6-7, 28 (Case No. C-05-05312 RMW), and all evidence of record relating to the claim construction proceeding in that case

'813 CLAIM TERM AT ISSUE	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
<p>"means...for rendering uniform the radial absorbed dose profile of the emissions from the one of the inner spatial volume and outer chamber containing the radionuclides" (claim 1)</p>	<p><i>function: making the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument</i></p> <p><i>structure: a radiation absorbing or attenuating material, e.g., air, x-ray contrast fluid, contrast media used in angiography, water, a gas, or barium sulfate or their equivalents</i></p>	<p>"Uniform"—"Always the same, as in character or degree, unvarying" (The American Heritage College Dictionary (3rd Ed. 1997), "AHD"))</p> <p>Abstract</p> <p>Col. 1:26-46</p> <p>Col. 1:50 – col. 2:3</p> <p>Col. 2:44-63</p> <p>Col. 3:14-38</p> <p>Col. 3:49 – col. 4:12</p> <p>Col. 4:21-31</p> <p>Col. 4:56-61</p> <p>Figs. 1, 3-5</p> <p>Notice of allowability (12-18-98) at 2</p> <p>September 8, 1998 Amendment at 3-7</p> <p>4-27-07 Claim Construction Order at 8-10, 28 (Case No. C-05-05312 RMW)), and all evidence of record relating to the claim construction proceeding in that case</p>
<p>"inner, closed chamber" (claim 2)</p>	<p>No construction necessary</p>	
<p>"plurality of radioactive solid particles" (claim 12)</p>	<p>No construction necessary</p>	
<p>"predetermined locations" (claim 12)</p>	<p>No construction necessary</p>	
<p>"plurality of radioactive solid particles placed at pre-determined locations" (claim 12)</p>	<p>No construction necessary</p>	

Exhibit B

EXHIBIT B
U.S. Patent No. 6,413,204

' 204 CLAIM TERM AT ISSUE	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
"inner spatial volume" (claims 1, 2, 3)	<i>a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere.</i>	Abstract Col. 2:7-33 Col. 2:36-68 Col. 3:19-45 Col. 3:57-65 Col. 3:66 – col. 4:5 Col. 4:4-14, 44-67 Col. 5:1-12 Col. 5:13-41 Col. 8:7-12 FIGS. 1, 3-7 June 20, 2000 Office Action at 3-5 December 20, 2000 Amendment at 8-19 4-27-07 Claim Construction Order at 3-5, 28 (Case No. C-05-05312 RMW)), and all evidence of record relating to the claim construction proceeding in that case 4-25-08 Order Denying Plaintiffs' Motion For Preliminary Injunction at 6-8

‘ 204 CLAIM TERM AT ISSUE	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
“outer spatial volume” (claims 1, 2, 17)	<i>a region of space defined by an expandable surface element and surrounding an inner spatial volume</i>	Abstract Col. 2:7-33 Col. 2:36-68 Col. 3:19-45 Col. 3: 61 – col. 4:8 Col. 2:61-67 Col. 4:4-10 Col. 5:13-65 Col. 8:7-12 FIGS. 1, 3-7 June 20, 2000 Office Action at 3-5 December 20, 2000 Amendment at 8-19 4-27-07 Claim Construction Order at 17 (Case No. C-05-05312 RMW)), and all evidence of record relating to the claim construction proceeding in that case
“three-dimensional isodose profile that is substantially similar in shape to the expandable surface element” (claim 1)	No construction necessary	

‘ 204 CLAIM TERM AT ISSUE	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
<p>“providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface” (claim 2)</p>	<p><i>controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target tissue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface</i></p>	<p>“Control” –“to hold in restraint, to check” (The American Heritage College Dictionary (3rd Ed. 1997), “AHD”))</p> <p>Abstract</p> <p>Col. 1:14 – col. 2:33</p> <p>Col. 2: 36-68</p> <p>Col. 2:46-51</p> <p>Col. 2: 63-67</p> <p>Col. 3: 1-16</p> <p>Col. 3:24-26</p> <p>Col. 3: 30-45</p> <p>Col. 5:13 – col. 7:5</p> <p>Col. 7:6-28</p> <p>Col. 8:7-12</p> <p>FIGS. 1, 3-7</p> <p>December 20, 2000 Amendment at 8-19</p> <p>4-27-07 Claim Construction Order at 23, 29 (Case No. C-05-05312 RMW)), and all evidence of record relating to the claim construction proceeding in that case</p>

‘ 204 CLAIM TERM AT ISSUE	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
“predetermined spacing...between said inner spatial volume and the expandable surface element” (claim 3)	<i>the distance between the inner spatial volume and the expandable surface element is determined in advance</i>	Abstract Col. 1:14 – col. 2:33 Col. 2:36-68 Col. 2:46-51 Col. 2:63-67 Col. 3:1-16 Col. 3:24-26 Col. 3:30-45 Col. 3:57 – col. 4:3 Col. 4:44-67 Col. 5:1-12 Col. 5:13 – col. 6:28 Col. 6:61 – col. 7:5 Col. 7:23-32 Col. 7:58-64 col. 8:7-12 Figs. 1, 3-7 December 20, 2000 Amendment at 8-19 4-27-07 Claim Construction Order at 24-25, 29 (Case No. C-05-05312 RMW)), and all evidence of record relating to the claim construction proceeding in that case
“plurality of solid radiation sources” (claim 17)	No construction necessary	

‘ 204 CLAIM TERM AT ISSUE	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
“isodose profile having a shape substantially similar to the shape of the outer spatial volume” (claim 17)	No construction necessary	

Exhibit C

EXHIBIT C
U.S. Patent No. 6,482,142

'142 CLAIM TERM AT ISSUE ¹	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
<p>[three-dimensional] apparatus volume [configured to fill an interstitial void] (claims 1, 6)</p>	<p><i>A three-dimensional geometric solid composed of an expandable outer surface</i></p>	<p>Abstract Col. 2:20-53 Col. 2:60-64 Col. 3:20-36 Col. 3:55-62, 66-67 Col. 4: 1-2 Col. 4:27-42 Col. 5:36-65 Col. 6:11-29 Col. 8:1-32 Col. 8:52-59 FIGS 1, 3, 4 February 27, 2002 Amendment at 6-10 4-25-08 Order Denying Plaintiffs' Motion For Preliminary Injunction at 13-16</p>

¹ Hologic believes that construction of the term(s) identified by SenoRx require(s) construction of the entire phrase in which the term appears. Thus, the preliminary construction proposed by Hologic construes the phrase identified by SenoRx in the context of the additional terms highlighted within brackets.

'142 CLAIM TERM AT ISSUE ¹	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
located so as to be spaced apart from the apparatus volume (claim 1)	<i>located so as to be not on or touching the apparatus volume</i>	Abstract Col. 2:20-53 Col. 3:20-25, 55-62, 66-67 Col. 4: 1-2 Col. 4: 27-30, 35-57 Col. 5:36-65 Col. 6:11-29 Col. 7:1-15 Col. 7: 49-55 Col. 8:1-32 Col. 8:52-59 FIGS 1, 3, 4 February 27, 2002 Amendment at 6-10 4-25-08 Order Denying Plaintiffs' Motion For Preliminary Injunction at 13-16

'142 CLAIM TERM AT ISSUE ¹	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
asymmetrically located and arranged within the expandable surface (claim 1)	<i>Located and arranged so as not to be on the longitudinal axis of the expandable surface</i>	Abstract Col. 2:20-53 Col. 3:7-19 Col. 3:55-62, 66-67 Col. 4: 1-2 Col. 5:12-37 Col. 6:11-29 Col. 6:24-67 col. 7:1-15 Col. 8:1-32 Col. 8:52-59 FIGS 1, 3, 4 February 27, 2002 Amendment at 6-10

'142 CLAIM TERM AT ISSUE ¹	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
predetermined asymmetric isodose curves (claims 1, 6, 8)	<i>Predetermined isodose curves that are not symmetric with respect to the longitudinal axis of the apparatus volume</i>	Abstract Col. 2:20-53 Col. 2:60 – col. 3:1 Col. 3:7-19 Col. 5:12-37 Col. 6:11-29 Col. 6:24-67 Col. 7:28-48 Col. 7:62 – col. 8:3 Col. 8:1-32 Col. 8:52-59 February 27, 2002 Amendment at 6-10
plurality of solid radiation sources (claim 6)	No construction necessary	
being provided on at least two elongate members extending into the apparatus volume (claim 6)	No construction necessary	

'142 CLAIM TERM AT ISSUE ¹	PRELIMINARY CONSTRUCTION and IDENTIFICATION OF CORRESPONDING STRUCTURE	PRELIMINARY IDENTIFICATION OF INTRINSIC AND EXTRINSIC EVIDENCE
<p><i>[At least one of the elongate members]</i> being shaped to provide asymmetric placement of the radiation source with respect to a longitudinal axis <i>[through the apparatus volume]</i> (claim 6)</p>	<p><i>At least one elongate member is shaped so as to place the radiation source not on the longitudinal axis through the apparatus volume</i></p>	<p>Abstract Col. 2:20-53 Col. 3:7-19 Col. 3:55-62, 66-67 Col. 4: 1-2 Col. 5:11-35 Col. 6:11-29 Col. 6: 30-67 Col. 8:1-32 Col. 8:52-59 FIGS 1, 3, 4 February 27, 2002 Amendment at 6-10</p>

Exhibit 14

Lynn Verhey

Page 1

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

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HOLOGIC, INC., CYTYC CORPORATION,
and HOLOGIC L.P.,

Plaintiffs,

vs.

No. C08 00133 RMW (RS)

SENORX, INC.,

Defendant.

AND RELATED COUNTERCLAIMS.

DEPOSITION OF LYNN VERHEY

San Francisco, California

Wednesday, April 16, 2008

REPORTED BY:
LYNNE LEDANOIS
CSR No. 6811
Job No. 79773

Lynn Verhey

Page 2

1 UNITED STATES DISTRICT COURT
2 NORTHERN DISTRICT OF CALIFORNIA
3 SAN JOSE DIVISION
4 ---o0o---
5 HOLOGIC, INC., CYTYC CORPORATION,
6 and HOLOGIC L.P.,

7 Plaintiffs,
8 vs. No. C08 00133 RMW (RS)
9 SENORX, INC.,
10 Defendant.

11 AND RELATED COUNTERCLAIMS.
12
13

14 Deposition of LYNN JAMES VERHEY, taken on behalf of
15 Plaintiff, at 525 Market Street, Suite 3600, San
16 Francisco, California, beginning at 10:03 a.m. and
17 ending at 3:45 p.m. on Wednesday, April 16, 2008, before
18 LYNNE LEDANOIS, CSR 6811.
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<p>03:06:13 1 asymmetric with respect to the outer balloon?</p> <p>03:06:17 2 A Yes.</p> <p>03:06:24 3 Q Is it true, Dr. Verhey, that as of 1999, at</p> <p>03:06:29 4 least 1999, prior to inflating that inner balloon with a</p> <p>03:06:34 5 radioactive fluid, the profile that would be -- would</p> <p>03:06:40 6 result from doing so would have been calculated?</p> <p>03:06:44 7 A Yes.</p> <p>03:06:46 8 Q That's been true for decades now?</p> <p>03:06:49 9 MR. SU: Objection, form.</p> <p>03:06:51 10 THE WITNESS: For a long time.</p> <p>03:06:52 11 BY MR. MAURER:</p> <p>03:06:56 12 Q In your declaration, in paragraph 24, at line</p> <p>03:07:02 13 12 -- at the end of line 12, you have a sentence that</p> <p>03:07:08 14 starts, If the inner balloon has an asymmetry relative</p> <p>03:07:13 15 to the outer balloon --</p> <p>03:07:14 16 Do you see that?</p> <p>03:07:14 17 A Yes.</p> <p>03:07:15 18 Q -- that asymmetry is fixed by the geometric</p> <p>03:07:19 19 constraints of the device, and, therefore, the position</p> <p>03:07:21 20 of the inner balloon cannot be altered to provide</p> <p>03:07:24 21 predetermined isodose curve -- it does not say curve.</p> <p>03:07:34 22 Maybe it should, but it does not.</p> <p>03:07:39 23 What do you mean asymmetry fixed by geometric</p> <p>03:07:44 24 constraints of the device?</p> <p>03:07:50 25 A What I mean by that is, Williams does in the</p>	<p>03:10:04 1 A This will take a minute.</p> <p>03:10:05 2 Q Sure. Please.</p> <p>03:11:02 3 A It's all over the place.</p> <p>03:11:04 4 Q Okay. Let's start --</p> <p>03:11:05 5 A Column 3, the first complete paragraph. In</p> <p>03:11:13 6 other examples, the radiation source spaced apart is</p> <p>03:11:18 7 solid radioactive particles disposed within the</p> <p>03:11:21 8 apparatus volume and arranged to provide a predetermined</p> <p>03:11:24 9 asymmetric isodose curve within the target tissue.</p> <p>03:11:30 10 Q Does that describe a device in which the</p> <p>03:11:31 11 position of the radioactive particles can be changed?</p> <p>03:11:36 12 A Within the catheters, they could be changed.</p> <p>03:11:46 13 Q Is that an example that's depicted in one of</p> <p>03:11:48 14 the drawings?</p> <p>03:13:15 15 A Figure 3 as an example -- wait a minute. Let</p> <p>03:13:20 16 me see if 4 is a better example.</p> <p>03:14:05 17 Probably 4 is -- the last paragraph of column</p> <p>03:14:07 18 6.</p> <p>03:14:08 19 Q Okay.</p> <p>03:14:11 20 A An additional device 80 of the invention shown</p> <p>03:14:17 21 in Figure 4 includes a radiation source 82 that is made</p> <p>03:14:23 22 up of three wires, 84, 86, 88, each having a plurality</p> <p>03:14:29 23 of solid radiation particles. Wire 86 is a straight</p> <p>03:14:35 24 wire extending along the longitudinal axis 90 of the</p> <p>03:14:39 25 device, while wires 84 and 88 each curve, as wire 34</p>
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<p>03:07:54 1 indicate that the location of the center of the inner</p> <p>03:08:00 2 balloon is something that can be varied on a</p> <p>03:08:05 3 patient-to-patient basis. Therefore, the asymmetry you</p> <p>03:08:11 4 achieve would be determined by where it is rather than</p> <p>03:08:13 5 the asymmetry you may want to have on the basis of the</p> <p>03:08:19 6 tissues surrounding the cavity.</p> <p>03:08:29 7 Q Does the '142 patent require that the</p> <p>03:08:33 8 asymmetric dose be able to be changed in a device?</p> <p>03:08:42 9 MR. SU: Objection to form, calls for a legal</p> <p>03:08:44 10 conclusion.</p> <p>03:08:45 11 BY MR. MAURER:</p> <p>03:08:48 12 Q Do you have an opinion on that?</p> <p>03:08:52 13 A My opinion is that the '142 gives you a --</p> <p>03:08:57 14 describes a device in which the asymmetry of the</p> <p>03:09:04 15 resulting dose distribution can be managed by the</p> <p>03:09:08 16 position of the sources in the catheters.</p> <p>03:09:31 17 MR. MAURER: Let me mark as Exhibit Number 13</p> <p>03:09:34 18 the '142 patent.</p> <p>03:09:35 19 (Plaintiff's Exhibit 13 was marked for</p> <p>03:09:35 20 identification by the Court Reporter.)</p> <p>03:09:35 21 BY MR. MAURER:</p> <p>03:09:49 22 Q Dr. Verhey, where does the '142 patent, Exhibit</p> <p>03:09:54 23 13, describe a device in which the asymmetry can be</p> <p>03:09:59 24 managed by the position of the radiation source in the</p> <p>03:10:02 25 catheters?</p>	<p>03:14:46 1 described above with respect to Figure 1. Wires 84 and</p> <p>03:14:50 2 88 are coplaner resulting in an isodose profile 92 that</p> <p>03:14:57 3 is similar to size. Dose profile 64 of Figure 3A, that</p> <p>03:15:04 4 is, the isodose profile, will be symmetric in the plane</p> <p>03:15:08 5 in which wires 84 and 88 are disposed, will have areas</p> <p>03:15:12 6 of reduced dosage in areas transfers to that plain that</p> <p>03:15:16 7 is in Figure 4 the directions into and out of the page.</p> <p>03:15:21 8 As with the device 50 of Figures 3 and 3A,</p> <p>03:15:25 9 device 80 can be configured with more or fewer wires,</p> <p>03:15:29 10 84, 86 and 88, and can be provided in configurations</p> <p>03:15:35 11 other than the depicted coplaner configuration in order</p> <p>03:15:39 12 to desired asymmetric isodose profiles.</p> <p>03:15:44 13 Q That is what that section says, Dr. Verhey. My</p> <p>03:15:47 14 confusion is to how that describes a device in which the</p> <p>03:15:53 15 asymmetry of the radiation profile can be managed by the</p> <p>03:15:59 16 position of the wires and the catheters.</p> <p>03:16:05 17 A Why is that confusing?</p> <p>03:16:07 18 Q Isn't this section that you just read, isn't</p> <p>03:16:11 19 that properly read that there is a device such as that</p> <p>03:16:15 20 shown in Figure 4, or you can modify the device of</p> <p>03:16:19 21 Figure 4 into another device by removing one or more of</p> <p>03:16:26 22 the arms or the radioactive sources on those arms?</p> <p>03:16:31 23 A Yes.</p> <p>03:16:32 24 Q So what that passage is saying is that there</p> <p>03:16:35 25 are a multiplicity of devices that fall within this</p>

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<p>03:16:42 1 description, but not that those devices themselves are</p> <p>03:16:47 2 modifiable in order to manage the asymmetric profile?</p> <p>03:16:52 3 A I believe there are a multiplicity of</p> <p>03:16:56 4 embodiments of this invention which are being described,</p> <p>03:16:59 5 not a multitude of different inventions or different</p> <p>03:17:02 6 devices.</p> <p>03:17:02 7 Q And do you agree that for the embodiment that</p> <p>03:17:06 8 is shown in Figure 4, that the asymmetry is fixed by the</p> <p>03:17:12 9 geometric constraints of that device?</p> <p>03:17:16 10 A As well as by the activity of the sources</p> <p>03:17:17 11 within the wires.</p> <p>03:17:20 12 MR. SU: Objection, form.</p> <p>03:17:21 13 BY MR. MAURER:</p> <p>03:17:24 14 Q Is that a yes and --</p> <p>03:17:27 15 A Yes.</p> <p>03:17:30 16 Q And the device of Figure 3 is one in which the</p> <p>03:17:34 17 asymmetry is fixed by the geometric constraints of the</p> <p>03:17:37 18 device?</p> <p>03:17:40 19 MR. SU: Objection, form.</p> <p>03:17:42 20 THE WITNESS: It is fixed by both the location</p> <p>03:17:46 21 and the activities of the sources in that device.</p> <p>03:17:48 22 BY MR. MAURER:</p> <p>03:17:52 23 Q And the device of Figure 3 of the '774 patent,</p> <p>03:17:55 24 going back to Exhibit Number 12, is likewise --</p> <p>03:18:01 25 according to your opinion, the asymmetry is fixed by the</p>	<p>03:20:03 1 be used in the device of Figure 3?</p> <p>03:20:05 2 A Yes.</p> <p>03:20:06 3 Q Can the balloon -- the inner balloon of Figure</p> <p>03:20:11 4 3 be changed in its position in the outer balloon?</p> <p>03:20:15 5 A It is not at all clear to me that it can.</p> <p>03:20:18 6 Q Does the '774 patent discuss the use of</p> <p>03:20:24 7 different sizes of balloons?</p> <p>03:20:26 8 A Yes.</p> <p>03:20:27 9 Q And would a person of ordinary skill in the art</p> <p>03:20:30 10 understand that that applies to Figure 3?</p> <p>03:20:33 11 A Yes.</p> <p>03:20:34 12 Q And that it applies to the inner balloon as</p> <p>03:20:39 13 well as the outer balloon?</p> <p>03:20:41 14 A Yes.</p> <p>03:20:43 15 Q So in using a different size inner balloon, you</p> <p>03:20:46 16 can achieve a different asymmetric isodose profile in</p> <p>03:20:52 17 Figure 3 of the '774 patent; correct?</p> <p>03:20:56 18 MR. SU: Objection, form.</p> <p>03:20:57 19 THE WITNESS: I have to expand on my answer.</p> <p>03:21:00 20 yes.</p> <p>03:21:00 21 The ratio of doses as an example between, let's</p> <p>03:21:06 22 say, the bottom line of this figure here and a point on</p> <p>03:21:12 23 the wall of the surgical cavity up at the top, that</p> <p>03:21:17 24 ratio cannot be modified by using different activity</p> <p>03:21:21 25 fluids because the shape of the dose distribution is</p>
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<p>03:18:08 1 geometric constraints of the device; correct?</p> <p>03:18:13 2 A I'm not sure I would agree with the "likewise"</p> <p>03:18:16 3 statement you just said.</p> <p>03:18:19 4 Q That's where I think we're having a disconnect,</p> <p>03:18:21 5 Dr. Verhey.</p> <p>03:18:22 6 A Yes.</p> <p>03:18:23 7 Q What is it that you're trying to express in the</p> <p>03:18:26 8 statement in paragraph 24 that we started this</p> <p>03:18:28 9 conversation with that differentiates the embodiments --</p> <p>03:18:32 10 admittedly, there are many of them -- in the '142 patent</p> <p>03:18:38 11 from the embodiments of Figure 3 in the '774 patent?</p> <p>03:18:42 12 A Figure 3 of '774, the shape of the isodose</p> <p>03:18:52 13 distributions is completely fixed by the position of the</p> <p>03:18:57 14 inner surface of the inner balloon, the position of the</p> <p>03:19:03 15 inner balloon as well as the diameter. The -- excuse</p> <p>03:19:08 16 me. Take that back.</p> <p>03:19:10 17 The shape is determine purely by the location</p> <p>03:19:12 18 of that inner balloon, nothing more, whereas, in '142,</p> <p>03:19:21 19 the shape of the isodose lines can be modified by either</p> <p>03:19:27 20 using different embodiments of this device or different</p> <p>03:19:37 21 placement of the wires or different activities of the</p> <p>03:19:42 22 individual wires in order to produce a particular,</p> <p>03:19:46 23 desired asymmetric dosage region.</p> <p>03:19:55 24 Q Let's go back to the '774 patent.</p> <p>03:20:00 25 Can radioactive fluids of different activities</p>	<p>03:21:25 1 determined by the geometry.</p> <p>03:21:29 2 That ratio that you just described can be</p> <p>03:21:32 3 modified by using different size balloons, though, to a</p> <p>03:21:37 4 very minor extent. You can take an extended source and</p> <p>03:21:43 5 turn it into a point source and make some changes in</p> <p>03:21:53 6 that regard, but not in terms of sparing normal tissues</p> <p>03:22:01 7 of particular interest to you, I don't believe the</p> <p>03:22:05 8 versatility of changing the diameter of that balloon</p> <p>03:22:08 9 would be accurate in a clinical sense.</p> <p>03:22:10 10 Q Does the '142 patent require the sparing of</p> <p>03:22:14 11 critical tissues?</p> <p>03:22:16 12 A No.</p> <p>03:22:21 13 MR. SU: Objection to form.</p> <p>03:22:23 14 BY MR. MAURER:</p> <p>03:22:31 15 Q Let's go back to the '142 patent. In Figure</p> <p>03:22:37 16 1 --</p> <p>03:22:44 17 MR. MAURER: We need to change the tape.</p> <p>03:22:46 18 VIDEOGRAPHER: This is the end of videotape</p> <p>03:22:47 19 number two. We are now going off the video record. The</p> <p>03:22:49 20 time is 3:22 p.m.</p> <p>03:22:51 21 (Recess Taken.)</p> <p>03:25:27 22 VIDEOGRAPHER: This is the beginning of tape</p> <p>03:25:29 23 number three. We are back on the video record. The</p> <p>03:25:31 24 time is 3:25 p.m.</p> <p>03:25:31 25 BY MR. MAURER:</p>

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<p>03:25:33 1 Q Before we took our short break, Dr. Verhey, I</p> <p>03:25:35 2 was asking you to refer back to Exhibit 1, Figure 1.</p> <p>03:25:44 3 A Yes.</p> <p>03:25:45 4 Q Is the isodose profile depicted there</p> <p>03:25:49 5 asymmetric with respect to the longitudinal axis of that</p> <p>03:25:52 6 device?</p> <p>03:25:53 7 A Yes.</p> <p>03:25:57 8 Q What is the longitudinal axis of that device?</p> <p>03:26:00 9 A It's the center of the catheter.</p> <p>03:26:03 10 Q If you look at Figure 3, including Figure 3A,</p> <p>03:26:09 11 is the radiation profile set forth or -- let me start</p> <p>03:26:16 12 over again.</p> <p>03:26:17 13 Is the radiation profile that is provided by</p> <p>03:26:23 14 the embodiment of Figure 3 asymmetric with respect to</p> <p>03:26:23 15 the longitudinal axis of the device?</p> <p>03:26:40 16 A No, actually, it's not with respect to the</p> <p>03:26:42 17 longitudinal axis.</p> <p>03:26:46 18 Q What about with Figure 4?</p> <p>03:26:55 19 A Yes, it is in a sense if you cut through the</p> <p>03:26:58 20 center, you get a different distribution than if you cut</p> <p>03:27:02 21 through a different region which is away from the</p> <p>03:27:05 22 center.</p> <p>03:27:06 23 Q Which is the -- where is the longitudinal axis</p> <p>03:27:10 24 of Figure 4?</p> <p>03:27:11 25 A 90. So along any particular line the dose</p>	<p>03:29:50 1 which is the '204 patent -- you can leave Exhibit 13 in</p> <p>03:29:55 2 front of you as well.</p> <p>03:30:12 3 If you can turn to Figure 5 of the '204 patent.</p> <p>03:30:20 4 A Yes.</p> <p>03:30:20 5 Q You're laughing. Why are you laughing?</p> <p>03:30:23 6 A It looks pretty familiar.</p> <p>03:30:25 7 Q It's essentially identical in its depiction</p> <p>03:30:29 8 between the two patents; correct?</p> <p>03:30:33 9 A Correct.</p> <p>03:30:33 10 Q If you go to the section of the '204 patent</p> <p>03:30:36 11 that discusses Figure 5, which is at column 5 --</p> <p>03:30:42 12 A M-hm.</p> <p>03:30:42 13 Q -- at line -- starting at line 16, the '204</p> <p>03:30:50 14 patent says that is the absorbed dose within the target</p> <p>03:30:54 15 tissue at a point equidistant from the surface 36 of the</p> <p>03:30:59 16 outer spacial line of 34 should be substantially uniform</p> <p>03:31:03 17 and substantially in every direction.</p> <p>03:31:10 18 That's not describing an asymmetric isodose</p> <p>03:31:11 19 profile, is it?</p> <p>03:31:12 20 A No, it's not.</p> <p>03:31:16 21 Q In which one of these patents did they</p> <p>03:31:18 22 misdescribe Figure 5?</p> <p>03:31:19 23 A '142. Unless they used the wrong figure when</p> <p>03:31:27 24 they printed the paper.</p> <p>03:31:31 25 Q Let's go back to the '774 patent, which is</p>
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<p>03:27:16 1 above and below is going to be the same at different</p> <p>03:27:21 2 planes. Cutting through the longitudinal axis, the</p> <p>03:27:24 3 answer would be different, but still the same above and</p> <p>03:27:27 4 below.</p> <p>03:27:33 5 Q So with respect to the longitudinal axis, it is</p> <p>03:27:36 6 symmetric, but with respect to other axis, it may be</p> <p>03:27:40 7 asymmetric; is that accurate?</p> <p>03:27:41 8 A Yes.</p> <p>03:27:45 9 Q Does Figure 5 provide an asymmetric isodose</p> <p>03:27:49 10 profile?</p> <p>03:27:53 11 A No, it does not appear that it does.</p> <p>03:28:35 12 Q Now you're confused, Dr. Verhey, aren't you?</p> <p>03:28:37 13 A Yes.</p> <p>03:28:38 14 Q Because you're looking at the description of</p> <p>03:28:39 15 column 7 of Figure 5 --</p> <p>03:28:41 16 A I'm looking at exactly that.</p> <p>03:28:42 17 Q -- and that says it's asymmetric?</p> <p>03:28:45 18 A It says that. At least we agree on what the</p> <p>03:28:50 19 longitudinal axis is.</p> <p>03:29:00 20 Q A person of ordinary skill in the art looking</p> <p>03:29:02 21 at the embodiments of Figure 5 would understand that the</p> <p>03:29:05 22 radiation profile that would be generated by this</p> <p>03:29:08 23 embodiment would be symmetric; correct, not asymmetric?</p> <p>03:29:17 24 A That's what I'm thinking at the moment.</p> <p>03:29:48 25 Q In fact, Dr. Verhey, if you pick up Exhibit 2,</p>	<p>03:31:34 1 Exhibit 12.</p> <p>03:31:39 2 A Right.</p> <p>03:31:40 3 Q Is the radiation profile generated by the</p> <p>03:31:45 4 radiation source in the inner balloon asymmetric with</p> <p>03:31:49 5 respect to the longitudinal axis of that device?</p> <p>03:31:54 6 A No.</p> <p>03:31:56 7 Q Why not?</p> <p>03:31:57 8 A The longitudinal axis of the device is the axis</p> <p>03:32:01 9 which goes through the center of the catheter -- of the</p> <p>03:32:07 10 tube and through the center of the balloon. So with</p> <p>03:32:10 11 respect to that axis, the doses relative to the inner</p> <p>03:32:15 12 balloon are symmetric.</p> <p>03:32:19 13 Q Let me make sure we're not talking past each</p> <p>03:32:22 14 other again. Let me ask you to draw in my blue pen</p> <p>03:32:25 15 the -- I'm sorry -- the longitudinal axis of the device</p> <p>03:32:31 16 of Figure 3.</p> <p>03:32:32 17 A Well, actually, I need to ask you what you mean</p> <p>03:32:34 18 by "the device."</p> <p>03:32:39 19 Q By "the device" of Figure 3, I mean the device</p> <p>03:32:42 20 that's depicted in Figure 3.</p> <p>03:32:44 21 A The device has two balloons which are not</p> <p>03:32:48 22 concentric, and so which -- what do you call "the</p> <p>03:32:52 23 device"?</p> <p>03:32:54 24 Q That's a -- I understand your confusion now.</p> <p>03:32:58 25 Let's assume for purposes of this question that</p>

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<p>03:33:01 1 the device is everything shown in Figure 3 that is not</p> <p>03:33:05 2 the tissue --</p> <p>03:33:08 3 A Okay.</p> <p>03:33:08 4 Q -- whereas, the -- can you draw in the</p> <p>03:33:11 5 longitudinal axis of that device?</p> <p>03:33:13 6 A So you're really saying the longitudinal axis</p> <p>03:33:16 7 of the cavity?</p> <p>03:33:19 8 Q Well, what I'm asking -- it might be the same</p> <p>03:33:22 9 as the cavity. What I'm asking is for you to draw in</p> <p>03:33:25 10 the longitudinal axis.</p> <p>03:33:27 11 A If the device contains both balloons and the</p> <p>03:33:30 12 tubes which fill them, then that would be, in my</p> <p>03:33:34 13 opinion, the longitudinal axis.</p> <p>03:33:36 14 Q And you've drawn it there sort of down the</p> <p>03:33:38 15 middle of the two tubes?</p> <p>03:33:42 16 A Right.</p> <p>03:33:44 17 Q And I'll ask my prior question again.</p> <p>03:33:47 18 Using that as a longitudinal axis of the</p> <p>03:33:49 19 device, is the radiation profile that is generated by</p> <p>03:33:55 20 the radioactive fluid inside the inner balloon</p> <p>03:33:59 21 asymmetric with respect to that axis?</p> <p>03:34:02 22 A Yes.</p> <p>03:34:09 23 MR. SU: Objection to the whole line of</p> <p>03:34:09 24 questioning, incomplete hypothetical.</p> <p>03:34:12 25 BY MR. MAURER:</p>	<p>03:39:16 1 interesting in terms of the surgical cavity which is</p> <p>03:39:20 2 approximately filled by the outer balloon. So any --</p> <p>03:39:24 3 that's why I drew my longitudinal axis to be between the</p> <p>03:39:31 4 catheters and through the center of the outer balloon.</p> <p>03:39:35 5 Q If the cavity -- surgical cavity were roughly</p> <p>03:39:40 6 spherical, as I think there has been some discussion</p> <p>03:39:43 7 about, is there -- does a roughly spherical cavity have</p> <p>03:39:49 8 a longitudinal axis?</p> <p>03:39:52 9 MR. MAURER: Objection to form.</p> <p>03:39:58 10 THE WITNESS: I think so.</p> <p>03:39:59 11 BY MR. SU:</p> <p>03:40:01 12 Q How would you determine that?</p> <p>03:40:03 13 A By approximating the roughly spherical cavity</p> <p>03:40:09 14 as a sphere and then drawing something that represents</p> <p>03:40:13 15 the center of that.</p> <p>03:40:17 16 Q Which direction would you -- would the axis</p> <p>03:40:23 17 pierce the sphere?</p> <p>03:40:31 18 A I assumed it would be in the direction in which</p> <p>03:40:33 19 the catheters were being used, although there is no</p> <p>03:40:42 20 exact preference that -- I mean, it could be anything</p> <p>03:40:47 21 going through the approximate center of the cavity, in</p> <p>03:40:50 22 my opinion.</p> <p>03:40:54 23 Q Let's turn to Exhibit 13. I seem to recall a</p> <p>03:41:06 24 question from Mr. Maurer about whether the '142 requires</p> <p>03:41:14 25 the protection of critical tissue.</p>
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<p>03:34:19 1 Q With respect to the '774 patent -- never mind.</p> <p>03:34:31 2 MR. MAURER: No further questions at this time.</p> <p>03:34:33 3 But I would like my pen back.</p> <p>03:34:39 4 MR. SU: Dr. Verhey, I have some questions for</p> <p>03:34:41 5 you, but before we do that, do you need to take a break?</p> <p>03:34:44 6 THE WITNESS: I think I would like to take a</p> <p>03:34:46 7 quick break.</p> <p>03:34:47 8 VIDEOGRAPHER: We are now going off the video</p> <p>03:34:48 9 record. The time is 3:34 p.m.</p> <p>03:34:50 10 (Recess Taken.)</p> <p>03:38:31 11 VIDEOGRAPHER: We are now back on the video</p> <p>03:38:32 12 record. The time is 3:38 p.m.</p> <p>03:38:34 13 EXAMINATION</p> <p>03:38:34 14 BY MR. SU:</p> <p>03:38:36 15 Q Dr. Verhey, if you take a look at Exhibit 12,</p> <p>03:38:39 16 looking at Figure 3, which I think is right in front of</p> <p>03:38:43 17 you.</p> <p>03:38:43 18 A Give me a second.</p> <p>03:38:51 19 Q Does Figure 3 indicate anywhere by a line and</p> <p>03:38:53 20 reference numeral a longitudinal axis?</p> <p>03:38:56 21 A No.</p> <p>03:38:57 22 Q And is there any way to tell what would be a</p> <p>03:39:03 23 longitudinal axis?</p> <p>03:39:08 24 A I would answer that by saying that the -- in</p> <p>03:39:13 25 terms of the dosimetry, the longitudinal axis is</p>	<p>03:41:22 1 Do you recall that question?</p> <p>03:41:23 2 A Yes.</p> <p>03:41:24 3 Q And what was your answer to that question?</p> <p>03:41:27 4 A No.</p> <p>03:41:29 5 Q I would like to direct your attention to column</p> <p>03:41:32 6 2 of Exhibit 13, and there is a paragraph that starts</p> <p>03:41:42 7 about line 43, goes to line 53.</p> <p>03:41:48 8 A Yes.</p> <p>03:41:49 9 Q Do you see that?</p> <p>03:41:54 10 A Yes.</p> <p>03:41:54 11 Q Could you read that to yourself, please?</p> <p>03:42:03 12 A Yes.</p> <p>03:42:03 13 Q Does that paragraph say anything about</p> <p>03:42:05 14 protecting critical tissue?</p> <p>03:42:08 15 A Yes.</p> <p>03:42:13 16 Q And if you look at -- strike that.</p> <p>03:42:19 17 Let's now look at where we are. Now, let's go</p> <p>03:42:28 18 back to the Ashpole reference, which is Exhibit 6. I</p> <p>03:42:40 19 would like to turn your attention to page 336.</p> <p>03:42:48 20 Do you recall that Mr. Maurer asked you some</p> <p>03:42:52 21 questions about the sentence towards the top of the</p> <p>03:42:57 22 right-hand column, the second column --</p> <p>03:43:00 23 A Yes.</p> <p>03:43:00 24 Q -- where it reads, The dose that the surface of</p> <p>03:43:03 25 the balloon depends on the number and arrangement of</p>

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<p>03:43:06 1 sources, as well as the balloon diameter, and can be as</p> <p>03:43:10 2 high as 70 Gray?</p> <p>03:43:11 3 A Yes.</p> <p>03:43:13 4 Q Is it your testimony that under the device of</p> <p>03:43:19 5 Ashpole, that one can change the balloon diameter to</p> <p>03:43:25 6 modify the surface dose?</p> <p>03:43:29 7 A No, it's not my understanding of that.</p> <p>03:43:35 8 Q How would one modify the surface dose under</p> <p>03:43:38 9 Ashpole?</p> <p>03:43:42 10 A The number and arrangement of sources and</p> <p>03:43:47 11 patient selection in a sense that patients with larger</p> <p>03:43:52 12 surgical cavities would be able to have more favorable</p> <p>03:43:58 13 dose distributions.</p> <p>03:44:06 14 Q I would like to then now turn your attention to</p> <p>03:44:09 15 the -- some of the drawings you did. And I don't have</p> <p>03:44:14 16 the exact exhibit numbers from you, but I'm looking</p> <p>03:44:19 17 specifically at -- let's look at Exhibits -- the ones</p> <p>03:44:24 18 that you're holding on your left hand -- or were</p> <p>03:44:27 19 holding, Exhibit --</p> <p>03:44:29 20 A 3 and 4.</p> <p>03:44:31 21 Q 3 and 4, yes, please.</p> <p>03:44:32 22 I want to make sure the record is clear. You</p> <p>03:44:35 23 see in Exhibits 3 and 4 that you've drawn a couple of</p> <p>03:44:39 24 isodose profiles?</p> <p>03:44:40 25 A Yes.</p>	<p>1</p> <p>2</p> <p>3</p> <p>4</p> <p>5</p> <p>6</p> <p>7</p> <p>8</p> <p>9</p> <p>10</p> <p>11</p> <p>12</p> <p>13</p> <p>14</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>
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<p>03:44:41 1 Q Could you just draw an arrow linking those</p> <p>03:44:44 2 isodose profiles to the particular configurations to</p> <p>03:44:50 3 which they relate?</p> <p>03:44:51 4 A Yes. This one relates to the point source.</p> <p>03:45:03 5 Q And you're talking about Exhibit 3?</p> <p>03:45:05 6 A Exhibit 3, yes.</p> <p>03:45:08 7 Q Okay.</p> <p>03:45:08 8 A And this one was intended to be a 1 over R,</p> <p>03:45:13 9 flowing into a 1 over R square dependence, and,</p> <p>03:45:19 10 actually, it could be either of these configurations, as</p> <p>03:45:24 11 long as we're looking at this axis.</p> <p>03:45:26 12 But the easiest way to say it, it would be --</p> <p>03:45:29 13 an extended source would show that as close to the</p> <p>03:45:35 14 source, depending on the size of it, it would be 1 over</p> <p>03:45:37 15 R, and further away it would be 1 over R squared.</p> <p>03:45:41 16 MR. SU: That's all I have. Thank you.</p> <p>03:45:44 17 MR. MAURER: Nothing further.</p> <p>03:45:44 18 Thank you very much, Doctor.</p> <p>03:45:49 19 VIDEOGRAPHER: This concludes today's</p> <p>03:45:49 20 proceedings. The number of videotapes used was three.</p> <p>03:45:50 21 We are now going off the video record. The time is 3:45</p> <p>03:45:52 22 p.m.</p> <p>23 //</p> <p>24 //</p> <p>25</p>	<p>1</p> <p>2</p> <p>3</p> <p>4</p> <p>5</p> <p>6</p> <p>7</p> <p>8</p> <p>9 I, LYNN JAMES VERHEY, do hereby declare under</p> <p>10 penalty of perjury that I have read the foregoing</p> <p>11 transcript; that I have made any corrections as appear</p> <p>12 noted, in ink, initialed by me; that my testimony as</p> <p>13 contained herein, as corrected, is true and correct.</p> <p>14 EXECUTED this ____ day of _____,</p> <p>15 20__, at _____, _____.</p> <p>(City) (State)</p> <p>16</p> <p>17</p> <p>18</p> <p>19 LYNN JAMES VERHEY</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>

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